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SURGERY

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SURGERY

VOL. 31 FEBRUARY, 1952 NO. 2

Original Communications

THE BRONCHIAL ARTERIES

II. THEIR ROLE IN PULMONARY EMBOLISM AND INFARCTION

F. HENRY ELLIS, JR., M.D.,* JOHN H. GRINDLAY, M.D.,** AND JESSE E. EDWARDS, M.D.,*** ROCHESTER, MINN.

IT HAS long been assumed that the bronchial arterial circulation is essential for the nutrition of the normal lung. From an experimental study on dogs, however, we recently concluded that the bronchial arterial circulation is unnecessary for this purpose, and that pulmonary arterial blood is adequate for the nutrient requirements of the pulmonary parenchyma and the bronchial wall distal to the hilum.[1] The bronchial arteries are known to dilate in response to pathologic conditions of the lung,[2-11] and it would appear that these vessels play an important role in supplying the diseased lung with blood. This report is based on experiments carried out to investigate the role of the bronchial arteries in pulmonary embolism and infarction.

Virchow[3-5] was the first to point out the marked dilatation of the bronchial arteries that occurs after the production of pulmonary embolism in experimental animals, and he concluded that this extensive collateral circulation prevents the lung from undergoing infarction. Since Virchow's time, other investigators also have encountered dilated bronchial arteries, and, in certain instances, precapillary anastomoses between the pulmonary and bronchial arteries in the presence of chronic pulmonary embolism in experimental animals.[6, 7] These observations have led to the conclusion that the bronchial arterial circulation prevents pulmonary infarction after bland embolism of the normal lung. Presumably, occlusion of the bronchial arterial circulation to a pulmonary lobe might alter the response of that lobe to an embolus. If the bronchial arterial blood supply normally prevents infarction after bland embolism of the lung, one would expect infarction to occur in its absence. If some mechanism other than

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a collateral bronchial arterial circulation can prevent infarction after bland pulmonary embolism, occlusion of the bronchial arteries should have no effect on the involved lung.

EXPERIMENTAL PROCEDURES

The experimental procedures on which this report is based have been divided into 3 groups. In each group mongrel dogs which weighed between 11 and 14 kilograms were used. The bronchial arterial circulation to the right apical lobe was occluded by a technique described in a previous article.[1] Briefly, the technique consisted of the intra-arterial injection of a nonirritating plastic material (vinyl acetate) which becomes hard after injection and occludes the vessel and its branches, but does not traverse the capillaries. In that study it was shown that the bronchial arterial circulation to the right apical lobe of a dog's lung can be occluded without causing the death of the animal.

At the termination of each experiment, the animals were anesthetized and killed by exsanguination. Necropsy was performed as described in a previous communication.[1] The aorta was clamped at the level of the diaphragm, both axillary and both carotid arteries were ligated, and the trachea was clamped. One hundred cubic centimeters of a contrast medium consisting of 40 per cent of barium sulfate and 12.5 per cent of gelatin was injected into the ascending aorta. The contents of the thoracic cavity were removed, care being taken to prevent the escape of the suspension of barium sulfate and gelatin, and roentgenograms of the lungs were made.

Group 1. Occlusion of the Bronchial Artery to the Right Apical Lobe and Subsequent Production of Pulmonary Embolism.—Eleven dogs were used for the procedures in this group. Ten to 14 days after occlusion of the bronchial artery to the right apical lobe, pulmonary embolism was produced in the following manner. After the animal had been anesthetized with ether, the right jugular vein was exposed, and a glass tube was inserted into it. Sterile glass beads with a diameter of from 2.8 to 3.3 mm. were suspended in physiologic salt solution and injected into the vein through the glass tube. The glass beads produced no local reaction in the tissues and could be visualized roentgenographically. It was necessary to inject about 150 beads for some to lodge in the right apical lobe since the majority lodged in the cardiac and diaphragmatic lobes.

All of the 11 dogs that were used for this group of experimental procedures showed evidence of varying degrees of dyspnea after the injection of the glass beads. Otherwise, they tolerated the injection well if they survived the immediate postoperative period.

One dog was killed on the second day after the injection of the beads, and 2 were killed on the third day. In these 3 dogs the right apical lobes were entirely normal. One dog died of unknown causes on the third day after injection. Gross examination of the apical lobe of the right lung of this dog revealed small zones of hemorrhage, and microscopic examination of these zones disclosed evidence of hemorrhage and inflammation. In all 4 of these dogs there

was evidence that blood from the systemic circulation had not reached the right apical lobe after occlusion of the bronchial arteries supplying the lobe. On gross and microscopic examination, the plastic material injected at the time of bronchial arterial occlusion could be seen filling the lumina of these arteries. Roentgenograms of the lungs made after the injection of a suspension of barium sulfate and gelatin into the aorta revealed no radiopaque medium in the right apical lobe of any of these dogs. The remaining lobes in all instances showed an occasional zone of hemorrhage and slight dilatation of the bronchial arteries.

Five dogs were killed between 4 and 7 days after the injection of the glass beads. In 4 of the 5 dogs post-mortem roentgenograms of the lungs after the injection of a suspension of barium sulfate and gelatin into the aorta did not disclose any evidence of the radiopaque medium in the right apical lobe (Fig. 1, *a*). There were present in the other dog a few narrow bronchial arteries filled with radiopaque medium going to the right apical lobe. In all of these 5 dogs, the dilatation of the bronchial arteries of the remaining lobes was much more pronounced than it was in the 4 dogs which were killed or died 2 or 3 days after the injection of the glass beads.

The right apical lobe was entirely normal in all of these 5 dogs. Without exception, gross examination of the other lobes of both lungs revealed zones of hemorrhage (Fig. 1, *b*). Microscopic examination of some of these zones disclosed intra-alveolar hemorrhage and edema (Fig. 2, *a*). In other zones, the histologic picture was characteristic of true hemorrhagic infarction (Fig. 2, *b*). In all of these 5 dogs, such zones of infarction could be found in 1 or more of the cardiac and diaphragmatic lobes of both lungs. The emboli were far more numerous in these lobes than they were in the apical lobes. True infarcts, however, were present in the left apical lobe in 3 of the dogs.

Of the 2 remaining dogs which were used for the experimental procedures in this group, 1 was killed 11 days after the injection of the glass beads, and the other was killed on the sixteenth day. The right apical lobe of the first dog contained definite zones of hemorrhage and 1 infarct. Roentgenographic and gross and microscopic examination, however, disclosed a well-established collateral systemic circulation to the right apical lobe. In the second dog, the right apical lobe was normal, and similar studies indicated that systemic blood had not reached the right apical lobe. In both dogs, many small zones of hemorrhage were present in the remaining lobes. A yellowish brown discoloration, suggestive of old hemorrhage, and deposition of hemosiderin were evident in these zones. Microscopic examination disclosed healing of infarcts in some instances. Examination of these lobes revealed dilated bronchial arteries and precapillary anastomosis between the bronchial arteries and the pulmonary arterial system.

Group 2. Occlusion of the Bronchial Artery to the Right Apical Lobe and Division of One or Both Branches of the Pulmonary Artery to the Same Lobe.— The results of the experimental procedures in Group 1 suggested that a collateral pulmonary arterial circulation rather than a collateral bronchial arterial circulation is responsible for preventing infarction in the presence of bland pulmonary embolism. In the absence of a bronchial arterial circulation one

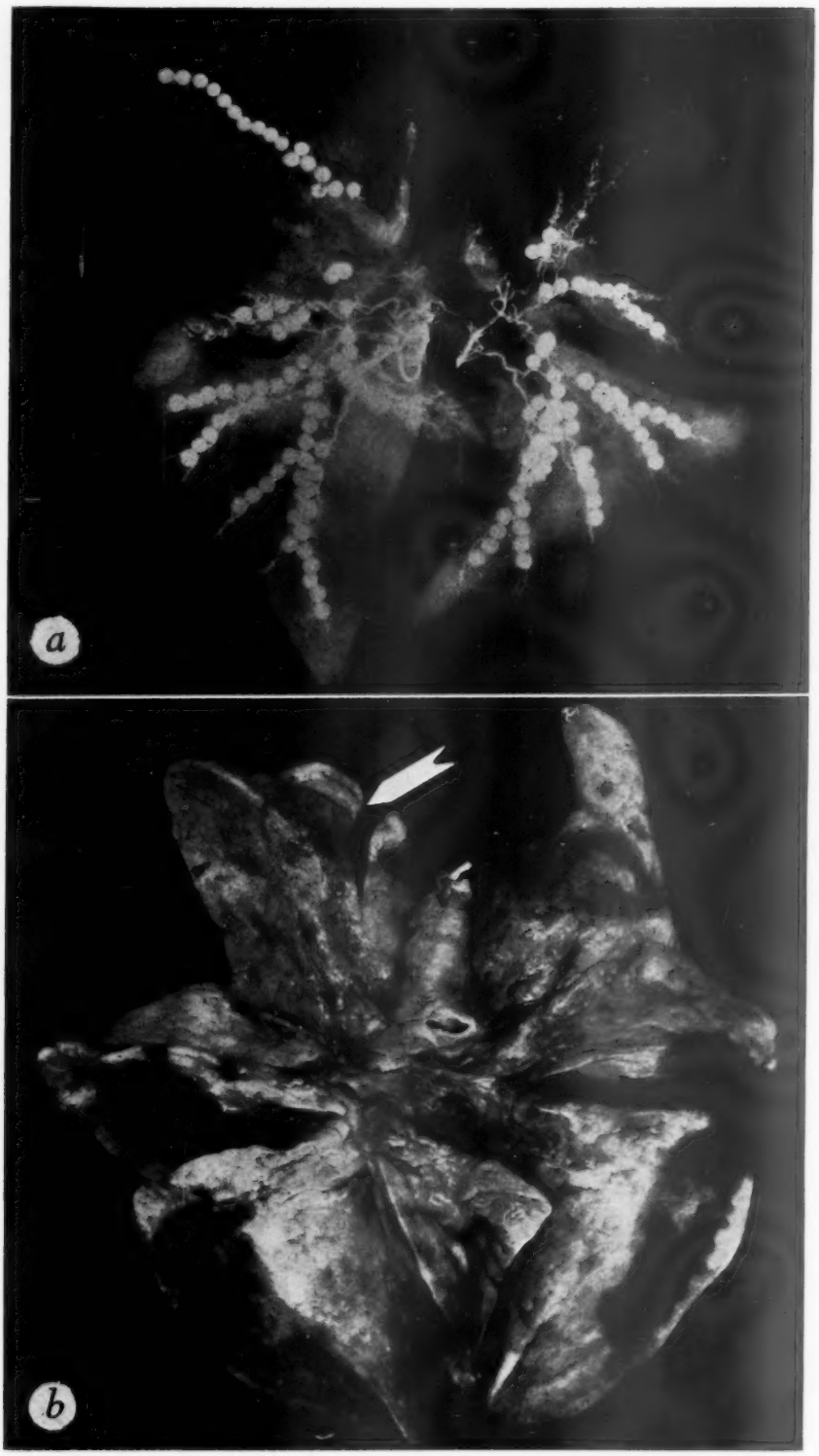

Fig. 1,*a*.—Post-mortem roentgenogram, from in front, of a dog's lungs 4 days after the injection of glass beads to produce pulmonary embolism. The right apical lobe bronchial artery was occluded 2 weeks previous to injection of the glass beads. A suspension of barium sulfate and gelatin outlines the bronchial arterial circulation. The absence of this circulation in the right apical lobe is demonstrated. Bronchial arteries markedly dilated in the other lobes. *b*.—Gross specimen of dog's lungs from in front. Experimental procedures as in dog whose lungs are illustrated in *a*. Pointer indicates lobe with occluded bronchial artery.

would expect infarction of a lobe to result if its main lobar pulmonary artery were divided. On the other hand, if a major branch of a lobar pulmonary artery were divided, the lobe would remain normal since it would be supplied by the remaining branches. The right apical lobe of the dog lends itself well to the following experimental procedures because it is supplied by 2 branches of the right pulmonary artery, and 1 of these branches can be divided without the necessity of intrapulmonary dissection with its accompanying complications.

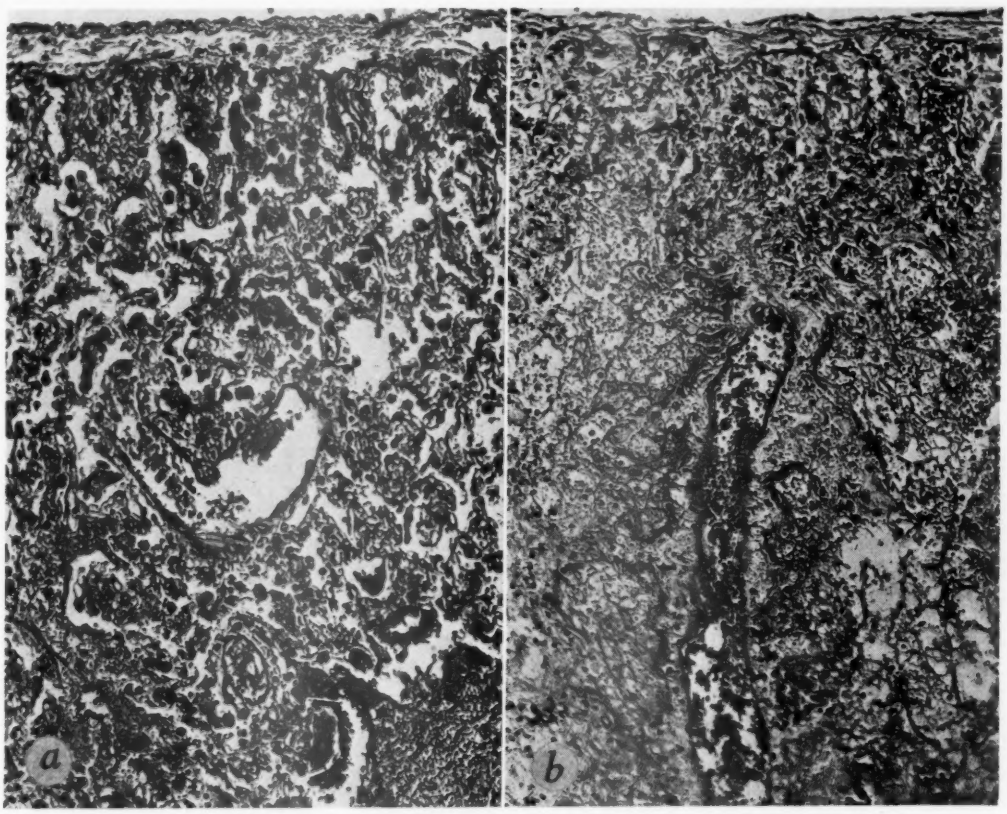

Fig. 2.—Photomicrographs of pulmonary tissue from dogs subjected to the same experimental procedure as described in legend of Fig. 1,*a*. Sections from lobes with intact bronchial arterial circulation. *a*.—Moderate intra-alveolar hemorrhage and edema (hematoxylin and eosin ×155); *b*.—hemorrhagic infarction (hematoxylin and eosin ×125).

In this way, one can accomplish experimentally what amounts to interruption of a major branch of a lobar pulmonary artery. Interruption of the entire pulmonary arterial circulation to the right apical lobe can be accomplished merely by dividing both of these branches. In this study the technique of interrupting the pulmonary arterial circulation to the right apical lobe consisted of dividing the vessels between silk ligatures.

Four dogs were used for the procedures in this group. In 2 of these animals, the bronchial arterial circulation to the right apical lobe was occluded and at the same time the entire pulmonary arterial circulation to the same lobe was interrupted. In both of these dogs, marked changes occurred in the right apical lobe. One of these 2 dogs was killed on the fourth day after completion

of the operative procedure, and the other one on the fourteenth day. In the dog which was killed on the fourth day, the right apical lobe was discolored (Fig. 3, *a*) and had a foul odor. Microscopic examination disclosed infarction and gangrene (Fig. 3, *b*). In the second dog, collateral systemic arteries to the right apical lobe were present, and examination of the lobe disclosed early healing of extensive infarction.

In the other 2 dogs, the bronchial arterial circulation to the right apical lobe was occluded, and, at the same time, one of the 2 lobar branches of the pulmonary artery to the same lobe was divided. When these animals were killed 7 and 14 days, respectively, after the operative procedure, examination did not disclose any change in the right apical lobe. A few collateral systemic vessels to the right apical lobe were evident in the animal which was killed 14 days after the operative procedure.

Group 3. Occlusion of the Bronchial Artery to the Right Apical Lobe, Production of Pulmonary Embolism, and Constriction of the Pulmonary Veins of Both Apical Lobes.—In the 11 dogs used for the experimental procedures in Group 1, infarcts did not occur in the right apical lobe after occlusion of its bronchial arterial circulation in the absence of collateral vessels to this lobe from the systemic circulation. Although infarcts frequently were present in the cardiac and diaphragmatic lobes of both lungs, in which the bronchial arterial circulation was intact, only 3 infarcts were noted in the left apical lobe in which this circulation was also intact. In analyzing the results of experimental procedures of this type, the right apical lobe should be compared with the left apical lobe and not with lower lobes in which emboli lodged in greater numbers and in which infarcts were more likely to occur. It was desirable, therefore, to compare the 2 apical lobes, one with and one without a bronchial arterial circulation, under conditions that normally could be expected to result uniformly in infarction after pulmonary embolism had been produced. This would give information on how much, if at all, the bronchial circulation contributes to the development of pulmonary infarction. Experimental evidence exists that pulmonary congestion favors the development of infarction after pulmonary embolism.[12-15] To produce pulmonary congestion of the right and left apical lobes, the pulmonary veins of these lobes were constricted after the intravenous injection of glass beads. Occlusion of the bronchial artery to the right apical lobe had been carried out 2 weeks previously in each case. Pulmonary venous constriction was carried out through an incision in the fourth intercostal space with the dog anesthetized by ether administered under intermittent positive pressure through an intratracheal tube. The pulmonary veins of both apical lobes were ligated with linen over a ligature carrier so that a lumen of 2.5 mm. was maintained after the ligature carrier was removed. This procedure was carried out bilaterally immediately after the production of pulmonary embolism as described previously.

The mortality following this combined procedure was high, as might be expected, and only 4 dogs lived for more than a few hours after the operation and were available for study at intervals of 4 to 10 days after the procedure.

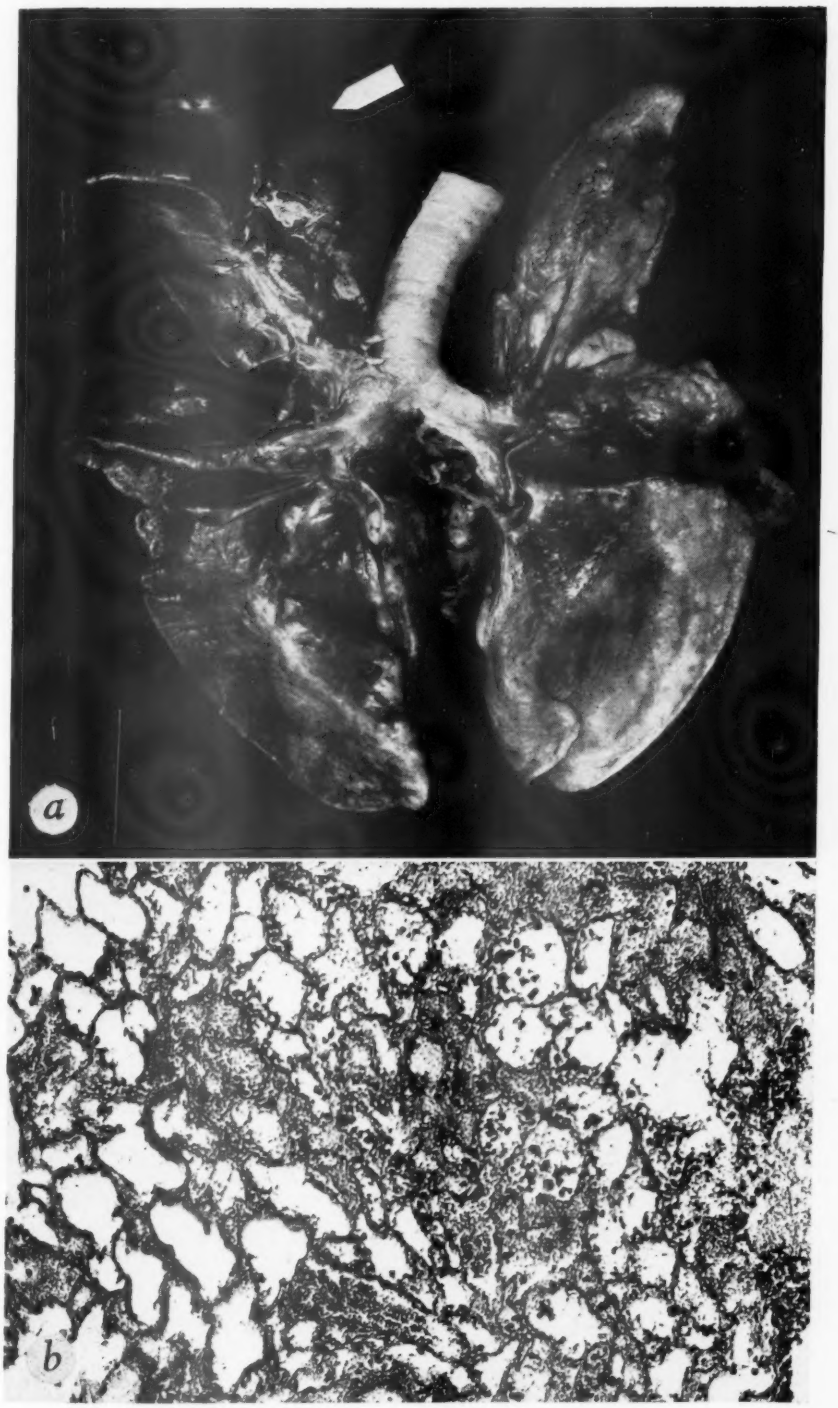

Fig. 3,*a*.—Gross appearance of dog's lungs from in front 4 days after occlusion of the bronchial and pulmonary circulations of the right apical lobe (pointer). This lobe was discolored, foul-smelling, and necrotic. *b*.—Photomicrograph of right apical lobe illustrated in *a* showing necrosis of tissue and distortion of normal cellular architecture (hematoxylin and eosin ×120).

In each case, infarcts were present in both apical lobes, regardless of whether or not the bronchial arterial circulation had been occluded (Fig. 4). In 2 dogs, there was no evidence of a systemic circulation to the lobe which had been deprived of its bronchial arterial circulation. In the remaining 2 dogs, a collateral systemic blood supply to this lobe was beginning to develop, although it was negligible in comparison with the increased bronchial arterial circulation to the opposite lobe.

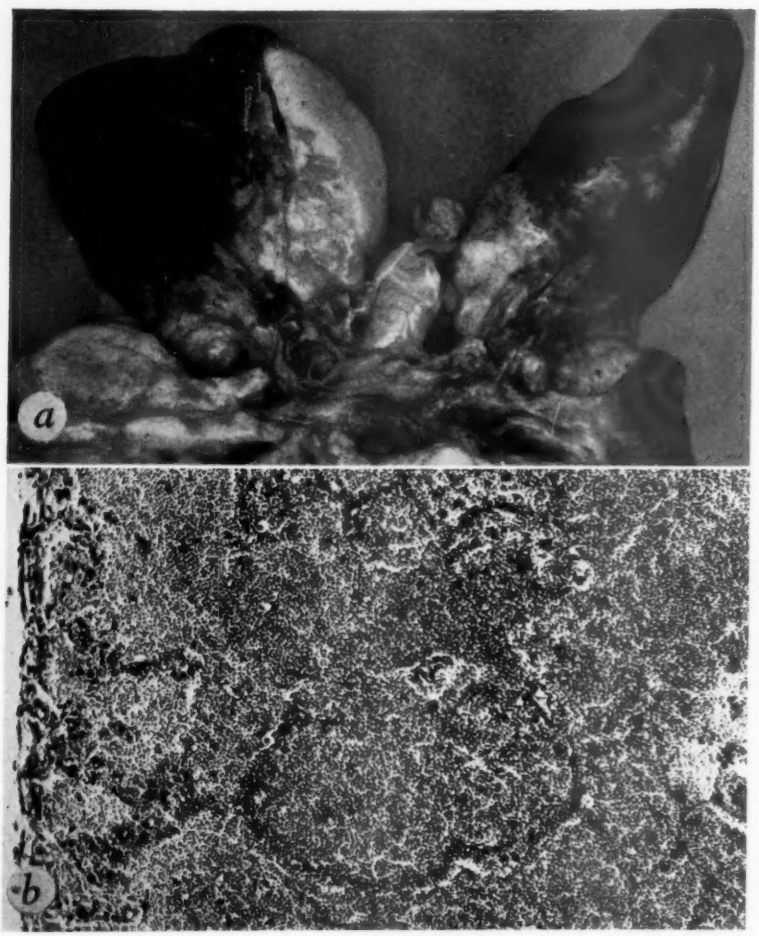

Fig. 4,*a*.—Gross specimen of right and left apical lobes from in front. Two weeks after occlusion of the bronchial artery to the right apical lobe the veins from each of the lobes were constricted and pulmonary embolism produced. Each of the apical lobes shows evidence of infarction. *b*.—Photomicrograph of one of the infarcts illustrated in *a* (hemotoxylin and eosin ×125).

It was impossible to detect any difference in the extent of infarction in those lobes that had an intact bronchial arterial circulation and in those lobes that had been deprived of this circulation.

COMMENT

As previously stated, it is the opinion of many investigators[3-5, 7, 16-19] that a collateral circulation supplied by the bronchial arteries prevents infarction

in the normal lung after bland pulmonary embolism. Karsner and his co-workers,[13, 20, 21] however, concluded from their experiments that preservation of the circulation distal to an embolism is not due to the collateral bronchial arterial circulation as much as it is to the free anastomosis and early division into capillaries of the pulmonary artery. These conclusions, however, were based on experiments in which the bronchial arterial circulation was interrupted by ligation.[13] This method has not proved successful in our hands or in the hands of other investigators.[6] The results of our experiments in which bronchial arterial occlusion was accomplished by the intra-arterial injection of a plastic material indicate that, in the dog, the bronchial arterial circulation is not necessary for the prevention of pulmonary infarction after pulmonary embolism, for in no instance was pulmonary infarction encountered in lobes which were the site of pulmonary embolism, and were without a bronchial arterial circulation. These results substantiate the views of Karsner and his co-workers regarding the importance of pulmonary capillary anastomoses in preventing pulmonary infarction after the induction of pulmonary embolism.

Confirmatory evidence for this hypothesis is offered by the results of the experimental procedures in Group 2, in which all or part of the pulmonary arterial blood supply to a lobe deprived of its bronchial arterial circulation was interrupted. Gangrene of the lobe occurred when the entire pulmonary arterial blood supply was interrupted whereas, when 1 of the 2 pulmonary arterial branches supplying the lobe was interrupted, the remaining lobar branch of the pulmonary artery sufficed for the nutrient requirements of the lobe.

The pulmonary arteries are end arteries, and no precapillary anastomoses exist[6, 22, 23]; therefore, for blood to reach the area distal to an embolus, it must do so through capillary anastomoses. Mathes and her co-workers[6] have shown that only fluid capable of passing through the pulmonary capillary bed will fill the area distal to a pulmonary embolus when injected into the pulmonary artery of a dog after death. By the intravenous injection of iodized oil into living dogs, Steinberg and Mundy[7] demonstrated that, even in the presence of multiple emboli, the region distal to the embolus frequently can be visualized. These studies indicate that circulation can occur in the area distal to an embolus through an anastomosis in the pulmonary capillary bed.

Most investigators[3-5, 13, 15, 24-26] have been unable to produce pulmonary infarction experimentally by bland pulmonary embolism alone. Conditions interfering with pulmonary arterial blood flow, such as pulmonary congestion,[12-15] pulmonary edema,[15] or pleural effusion,[13] must usually be present for infarction to develop. In the experimental procedures reported in this paper, true infarcts occasionally developed in lobes which maintained their bronchial arterial circulation and which contained multiple emboli. In the absence of true pulmonary infarcts, lesions exhibiting edema, alveolar hemorrhage and leucocytic infiltration corresponding to the "incomplete infarcts" described by Hampton and Castleman[27] were encountered. The fact that true infarction followed bland embolism alone is in agreement with the findings of Steinberg and Mundy,[7] who

demonstrated that, when sufficient emboli are present to produce complete obstruction of the pulmonary arterial blood supply to a segment of pulmonary tissue, infarcts occur. They believed that no factor other than embolism was necessary for the development of infarcts. It must be realized, though, that in the presence of such a large number of emboli the pulmonary arterial circulation is considerably impaired.

The results of the experimental procedures reported in this paper suggest that the bronchial arterial circulation is the source of the hemorrhage that occurs after pulmonary embolism. No hemorrhage occurred in the absence of a bronchial arterial circulation except in 1 case in which infection was a complicating factor. Furthermore, the hemorrhagic zones were not regularly encountered early, after production of pulmonary embolism when the bronchial arterial circulation was only slightly dilated; whereas, after four days, when this circulation had become markedly dilated, zones of hemorrhage occurred regularly. Other workers[6, 7] have encountered approximately the same sequence of events regarding the onset of bronchial arterial dilatation after pulmonary embolism.

The presence of hemorrhage into pulmonary tissue distal to an embolus can be explained on the basis of a high-pressure system emptying into a low-pressure area which is already subject to vascular alterations by the presence of some ischemia due to the interference with normal pulmonary arterial blood flow.

The zones of hemorrhage and edema that were observed in the absence of necrosis were typical of the so-called incomplete infarcts described by Hampton and Castleman.[27] When true infarcts occurred, in which necrosis of tissue was also present, they appeared to be a further extension of the morbid process taking place in these incomplete infarcts. Since in the experimental procedures in Group 1 no such areas were encountered in lobes lacking a bronchial arterial circulation, while so-called incomplete infarcts and true infarcts were present in the lobes with intact bronchial arteries, the evidence suggests that the intact and dilating bronchial arterial circulation may actually contribute to the development of infarcts after pulmonary embolism. However, from the results of the experimental procedures in Group 3, in which the pulmonary vein was constricted, it is evident that the bronchial circulation is not necessary for the development of pulmonary infarction if sufficiently severe pulmonary circulatory interference is present.

In interpreting the results of these experimental procedures, it must be remembered that a systemic blood supply to the right apical lobe became reestablished in certain instances. In only 1 instance, however, did it approach in size the bronchial arteries of the remaining lobes. The interpretation of results, then, although not as significant in these cases as it would have been if no systemic blood had been available to the lobe, is still valid. In the 1 animal in which an extensive systemic blood supply did develop after occlusion of the bronchial artery to the apical lobe of the lung, zones of hemorrhage and a true infarct were present in this lobe.

Finally, if the bronchial arterial circulation produces zones of hemorrhage after pulmonary embolism, why do these not occur after obstruction of a main lobar pulmonary artery by ligation? Schlaepfer[28] encountered a few zones of hemorrhage after such procedures in dogs, and they were situated in those regions in which a collateral blood supply through the bronchial artery had been established. Most authors[6, 29-31] have not observed such changes. When a lobar pulmonary artery is ligated, the precapillary anastomoses that develop between bronchial and pulmonary arteries transform the latter into a diverticulum of the bronchial artery.[31] In this way, a large portion of the pulmonary arterial bed is open to the bronchial circulation, and the impact of the systemic arterial pressure is absorbed before the alveoli are reached. In the presence of an embolus, a low pressure is produced in a small area. The dilated bronchial arteries, through precapillary anastomoses with the pulmonary arteries, now find the main pulmonary arterial tree full of circulating blood and tend to pour blood into the area in which the pressure is lowest. The cushioning effect of the vast pulmonary arterial bed is not available and the systemic pressure of the bronchial arterial system is concentrated on the small low-pressure area distal to the embolus. Hence the stage is set for the development of a focus of intra-alveolar hemorrhage and edema.

SUMMARY

The prevailing opinion in the literature appears to be that the dilatation of the bronchial arteries that follows pulmonary embolism supports the nutrient requirements of the pulmonary tissue distal to an embolus. A series of experiments was carred out to determine whether or not the bronchial arteries play a role in pulmonary embolism and infarction.

In 1 series of experiments, occlusion of the bronchial artery to the apical lobe of the lung was followed 2 weeks later by the production of pulmonary embolism. No pathologic changes were encountered after pulmonary embolism in lobes which had been deprived of their bronchial arterial circulation and in which a collateral systemic circulation had not developed. On the contrary, in lobes in which intact and dilated bronchial arteries were present after pulmonary embolism, zones of hemorrhage and edema resembling the incomplete infarcts described by Hampton and Castleman[27] occurred, and, when sufficient emboli were present, true pulmonary infarcts were encountered.

In another group of dogs, interruption of the entire pulmonary arterial blood flow to a lobe deprived of its bronchial arterial circulation was followed by gangrene of the lobe. When only one of the two pulmonary arterial branches to such a lobe was divided no detectable changes occurred.

A final group of experiments demonstrated that infarction occurred in lobes containing emboli when pulmonary venous congestion was present, regardless of the presence or absence of intact bronchial arterial circulation.

CONCLUSIONS

1. The nutrient requirements of pulmonary tissue distal to an embolus may be supported by the pulmonary arterial circulation through capillary anasto-

moses in the pulmonary capillary bed. The bronchial arterial circulation is not necessary for this purpose.

2. The hemorrhage that occurs into pulmonary tissue after pulmonary embolism may come from the bronchial arterial circulation.

3. The bronchial arterial circulation may actually be a contributing factor to the development of pulmonary infarction after pulmonary embolism.

4. The bronchial arterial circulation, however, is not necessary for the development of pulmonary infarction after pulmonary embolism, provided sufficiently severe pulmonary congestion is present.

REFERENCES

1. Ellis, F. H., Jr., Grindlay, J. H., and Edwards, J. E.: The Bronchial Arteries. I. Experimental Occlusion, SURGERY **30**: , 1951.
2. Guillot, M. N.: Sur une formation de vaisseaux dépendant de l'appareil respiratoire chez les phthisiques, Compt. rend. Acad. d. sc. **6**: 165-166, 1838.
3. Virchow, R.: Ueber die Standpunkte in der wissenschaftlichen Medicin, Virchow's Arch. f. path. Anat. **1**: 1-19, 1847.
4. Virchow, R.: Ueber die Erweiterung kleinerer Gefässe. Virchow's Arch. f. path. Anat. **3**: 427-462, 1851.
5. Virchow, Rudolf: Gesammelte Abhandlungen zur wissenschaftlichen Medicin, Frankfurt a. M., 1856, Experiment XX, Meidinger Sohn & Comp., pp. 285, 294-296.
6. Mathes, Mary E., Holman, Emile, and Reichert, F. L.: A Study of the Bronchial, Pulmonary, and Lymphatic Circulations of the Lung Under Various Pathologic Conditions Experimentally Produced, J. Thoracic Surg. **1**: 339-362, 1932.
7. Steinberg, Bernhard, and Mundy, C. S.: Experimental Pulmonary Embolism and Infarction, Arch. Path. **22**: 529-542, 1936.
8. Wood, D. A., and Miller, Miriam: The Role of the Dual Pulmonary Circulation in Various Pathologic Conditions of the Lungs, J. Thoracic Surg. **7**: 649-670, 1938.
9. Wright, R. D.: The Blood Supply of Abnormal Tissue in the Lungs, J. Path. & Bact. **47**: 489-499, 1938.
10. Liebow, A. A., Hales, M. R., and Lindskog, G. E.: Enlargement of the Bronchial Arteries, and Their Anastomoses With the Pulmonary Arteries in Bronchiectasis, Am. J. Path. **25**: 211-232, 1949.
11. Marchand, Paul, Gilroy, J. C., and Wilson, V. H.: An Anatomical Study of the Bronchial Vascular System and Its Variations in Disease, Thorax **5**: 207-221, 1950.
12. Zahn, F. W.: Experimentelle Erzeugung von Leber- und Lungeninfarkten, Zentralbl. f. allg. Path. u. path. Anat. **8**: 860, 1897.
13. Karsner, H. T., and Ash, J. E.: Studies in Infarction. II. Experimental Bland Infarction of the Lung, J. Med. Research **27**: 205-224, 1912.
14. Moses, Campbell: Role of Stasis in the Development of Pulmonary Infarcts, Arch. Path. **41**: 319-321, 1946.
15. Chapman, D. W., Gugle, L. J., and Wheeler, P. W.: Experimental Pulmonary Infarction; Abnormal Pulmonary Circulation as a Prerequisite for Pulmonary Infarction Following an Embolus, Arch. Int. Med. **83**: 158-163, 1949.
16. Westermark, Nils: On the Roentgen Diagnosis of Lung Embolism, Acta radiol. **19**: 357-372, 1938.
17. Bruner, H. D.: The Bronchial Artery in Pulmonary Infarction, North Carolina M. J. **8**: 306-310, 1947.
18. Shapiro, Robert, and Rigler, L. G.: Pulmonary Embolism Without Infarction, Am. J. Roentgenol. **60**: 460-465, 1948.
19. Kjellberg, S. R., and Olsson, S.-E.: Roentgenological Studies of Experimental Pulmonary Embolism Without Complicating Infarction in Dog, Acta radiol. **33**: 507-514, 1950.
20. Ghoreyeb, A. A., and Karsner, H. T.: A Study of the Relation of Pulmonary and Bronchial Circulation, J. Exper. Med. **18**: 500-506, 1913.
21. Karsner, H. T., and Ghoreyeb, A. A.: Studies in Infarction. III. The Circulation in Experimental Pulmonary Embolism, J. Exper. Med. **18**: 507-511, 1913.
22. Cohnheim, Julius: Untersuchungen über die embolischen Processe, Berlin, 1872, A. Hirschwald, 112 pp.
23. Konaschko, P. J.: Ueber Anastomosen zwischen der A. pulmonalis und den Aa. bronchiales, Ztschr. f. Anat. u. Entwcklngsgesch. **78**: 136-147, 1926.
24. Cohnheim, J., and Litten, M.: Ueber die Folgen der Embolie der Lungenarterien. Virchow's Arch. f. path. Anat. **65**: 99-115, 1875.

25. Dunn, J. S.: The Effects of Multiple Embolism of Pulmonary Arterioles, Quart. J. Med. 13: 129-147, 1920.
26. Hall, G. E., and Ettinger, G. H.: An Experimental Study of Pulmonary Embolism, Canad. M. A. J. 28: 357-368, 1933.
27. Hampton, A. O., and Castleman, Benjamin: Correlation of Postmortem Chest Teleroentgenograms With Autopsy Findings; With Special Reference to Pulmonary Embolism and Infarction, Am. J. Roentgenol. 43: 305-325, 1940.
28. Schlaepfer, Karl: Ligation of the Pulmonary Artery of One Lung With and Without Resection of the Phrenic Nerve; Experimental Study, Arch. Surg. 9: 25-94, 1924.
29. Horine, C. F., and Warner, C. G.: Experimental Occlusion of the Pulmonary Artery; An Anatomic Study, Arch. Surg. 28: 139-149, 1934.
30. Lindskog, G. E., and Gilman, Alfred: Effect of Pulmonary Artery Ligation on the Histamine Content of Lung, With Observations on Concomitant Structural Changes, Am. J. Physiol. 152: 417-422, 1948.
31. Liebow, A. A., Hales, M. R., Bloomer, W. E., Harrison, William, and Lindskog, G. E.: Studies on the Lung After Ligation of the Pulmonary Artery. II. Anatomical Changes, Am. J. Path. 26: 177-195, 1950.

STUDIES WITH ARTERIOVENOUS FISTULAS

II. Influence of Posture Upon Volume Flow

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IN A recent clinical study of the cardiac frontal area in a large group of patients with traumatic arteriovenous fistulas of relatively short duration there was demonstrable evidence of enlargement of the heart in approximately half, and a measurable reduction in heart size was noted after operative obliteration of the fistula in a comparable percentage.[1] It was felt that this study permitted certain conclusions regarding factors important in bringing about increase in heart size in the presence of an arteriovenous fistula. For one thing, the rapidity of development and the degree of cardiac enlargement seemed definitely related to the size of the fistula and the size of the vessels involved. For another thing, there was a definite relationship between the duration of the fistula and the enlargement of the heart. Still another factor of real importance was the location of the fistula with respect to whether it was caudad or cephalad to the heart. Patients with fistulas in the pelvis and lower extremities were much more prone to develop significant early increase in heart size than were patients with fistulas of the head, neck, shoulders, and arms. The present investigation was undertaken in the hope of throwing some light upon the explanation of this last interesting observation.

METHODS

Healthy mongrel dogs were used. Large side-to-side femoral arteriovenous fistulas were created surgically. The blood flow studies were made from two to five weeks later. After the induction of anesthesia by the intravenous administration of pentobarbital sodium, 35 mg. per kilogram of body weight, the dogs were placed supine on a tilt table. This table was so constructed that its center served as the fulcrum allowing for easy elevation of the head and lowering of the foot to an angle of 45 degrees or lowering of the head and elevation of the foot to the same angle. The dogs were placed in a position so that the heart was at the center of the table.

The area of the fistula was carefully exposed without injury to the vessels. Following the intravenous administration of heparin, the proximal femoral vein was isolated and divided. The severed ends were cannulated and connected to a vertical rotary flow meter. The rotometer was fixed to the table in such a fashion that it would remain at the level of the fistula throughout the study. Continuous measurement of the mean arterial pressure was made with a mercury

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manometer attached to the carotid or the contralateral femoral artery or both, and in some instances, to the aortic arch by means of a plastic tube passed into it through the carotid artery. In four dogs venous pressure of the distal vena cava was measured with a water manometer. In certain animals, suitable apparatus was attached to the carotid cannula for withdrawal or introduction of blood in order to maintain a constant level of pressure.

After blood pressure and blood flow through the proximal vein had become stabilized with the animal in the horizontal position, the table was tilted with the head either up or down. The level of blood pressure and the volume flow through the vein were recorded at frequent intervals. After pressure and volume flow had become stabilized, the table was returned to the horizontal position. In some instances the animal was left in each position for ten minutes, in others for fifteen minutes, but most commonly for twenty minutes. The table was then tilted in the opposite direction. Again after stabilization of blood pressure and volume flow through the proximal vein the table was returned to the horizontal position. Not infrequently, observations made in the various positions were repeated several times. In the case of two animals they were repeated after complete lumbar sympathetic denervation had been carried out on the side of the fistula, while in a third the only studies done were after sympathectomy. In another instance they were repeated after ligation of the vein distal to the site of the fistula. In those experiments in which an effort was made to keep the blood pressure constant, blood was withdrawn or infused intra-arterially, as was necessary. The rotometer was calibrated by passing heparinized dog's blood through it at various measured rates of flow.

RESULTS

In the first part of the investigation the animals were studied after bilateral carotid sinus denervation but without other effort to maintain a constant blood pressure. Unfortunately, of seven animals studied, relatively constant blood pressure was maintained in only one. The others exhibited wide fluctuations of pressure. The pressure was generally noted to rise when the head was tilted down, and to fall when the head was elevated. In addition, the pressure tended to vary widely in any given position from one part of the experiment to another. Since volume flow through the fistula was obviously related to blood pressure, these studies were considered unsuitable for analysis, with the exception of the observations made upon the one animal referred to. In the latter part of the study an effort was made to maintain the central aortic arch or carotid pressure at a constant level by withdrawal or reintroduction of blood intra-arterially.

Alterations in the volume of blood flow through the proximal vein were rather similar in all the experiments. When the head was elevated there was a tendency for an increase in blood flow through the vein, and when the head of the animal was made dependent the volume of blood flow decreased (Table I). The magnitude of the volume flow through the fistula, and the amount of change in the volume flow with alteration of the animal's position varied widely, depending at least in part upon the size of the animal, the size of the femoral

vessels, the size of the fistula, and the height of the blood pressure. Maximal flow through the proximal vein ranged in six of the seven dogs from approximately 300 to as much as 1,250 c.c. per minute. In the exceptional animal the volume flow was smaller.

TABLE I. CHANGES IN BLOOD FLOW THROUGH FEMORAL VEIN PROXIMAL TO ARTERIOVENOUS FISTULA WITH CHANGE IN POSITION OF ANIMAL*

NUMBER OF ANIMAL	CONSISTENCY OF MEAN CAROTID OR AORTIC ARCH PRESSURE	INCREASE IN FEMORAL BLOOD FLOW WITH HEAD ELEVATED	DECREASE IN FEMORAL BLOOD FLOW WITH HEAD DEPENDENT	REMARKS
1	Excellent	Yes	Yes	Fistula 1 cm. long, one month old; carotid sinus denervated
2	Excellent	Yes	Yes	Fistula 0.5 cm. long, one month old; same flow changes after lumbar sympathectomy
3	Good	Yes	Yes	Fistula one month old; same flow changes after lumbar sympathectomy
4	Good	Yes	Yes	Fistula 0.5 cm. long, one month old
5	Excellent	No change	Yes	Fistula 0.7 cm. long, 2 weeks old
		Yes	Yes	After ligation distal vein
6	Excellent	Yes	Yes	
7	Good	No change	Yes	Fistula 0.7 cm. long, 3 weeks old
8	Fair	Yes	Yes	Fistula 0.6 cm. long, one month old; lumbar sympathectomy

*In all except the first animal, central carotid or aortic arch pressure was maintained at a nearly constant level by intra-arterial transfusion or withdrawal of blood.

In Fig. 1 are charted the changes in volume flow with change in position in the case of a large (18.2 kilograms) animal with a large fistula. The study was carried out after carotid sinus denervation and without intra-arterial transfusion. It will be noted that the carotid blood pressure remained fairly constant and at a rather high level. Volume of blood flow through the proximal vein ranged between 1,000 and 1,075 c.c. per minute in the horizontal position, rose abruptly to 1,250 c.c. per minute when the head was elevated, and after falling to 990 c.c. per minute in the horizontal position, fell still further to 800 c.c. when the head was lowered and the hind extremities elevated. The difference between the volume of blood flow with the head down and head up was very great. Indeed the values in the latter position were 56 per cent greater than in the former. After the study recorded in this figure was completed it was repeated with similar and only slightly less striking alterations.

In Fig. 2 are charted data from a similar experiment performed upon a smaller animal (12.7 kilograms) with a smaller fistula and one in which the carotid blood pressure was maintained constantly at a mean pressure of about 85 mm. of mercury. The changes were of the same sort, though the volume of blood flow through the proximal vein and the changes in it were of smaller magnitude than in the other animal. In the horizontal position the volume flow

was 250 c.c. per minute, with the head elevated it was 275 c.c. per minute, and with the hind limbs elevated it was 200 c.c. per minute. Again the difference in blood flow in these two positions was considerable, the former being 37.5 per cent greater than the latter. In this experiment in which the carotid pressure was kept constant it will be seen that the femoral pressure rose when the hind limbs were dependent, and fell when they were elevated. Similar changes were observed in six other animals in which such observations were made (Table II).

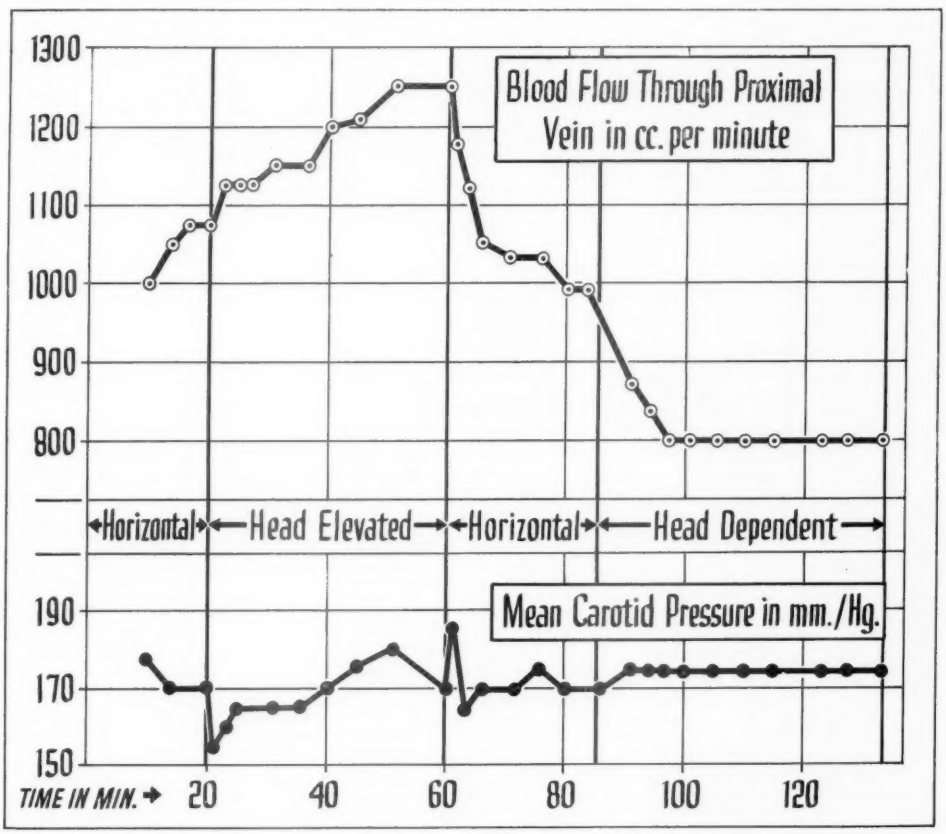

Fig. 1.—Chart showing alterations in blood flow through the proximal vein with change of position of Dog 1. Mean carotid pressure remained relatively stable.

Changes in the venous pressure of the distal vena cava also rose and fell with change in position. In the four dogs in which such observations were made the values were rather similar. The mean pressure in these animals was 6 cm. of water in the horizontal position, 18 cm. when the head was elevated and the hind limbs dependent, and –4.5 cm. in the reverse position. These changes are less than the changes in femoral arterial pressure, the mean extremes varying 22 cm. of water, or 16.5 mm. of mercury, while similar values for arterial pressure varied about 33 mm. of mercury. The difference in values in the two dogs in which distal vena caval and femoral arterial pressures were made simultaneously were of the same order as these mean values. In these animals differences in arterial pressure in the head-up and head-down positions

were 35 and 36 mm. of mercury respectively, while the differences in the venous pressures were 22 and 16 mm. of mercury respectively.

In the case of the three dogs in which observations were made upon the volume flow through the proximal vein following homolateral sympathetic denervation, changes with alteration in position similar to those which occurred with intact innervation were noted. No significant change in volume of blood flow through the proximal vein was noted to follow sympathectomy in the case of the two animals in which flow estimates were made immediately before and

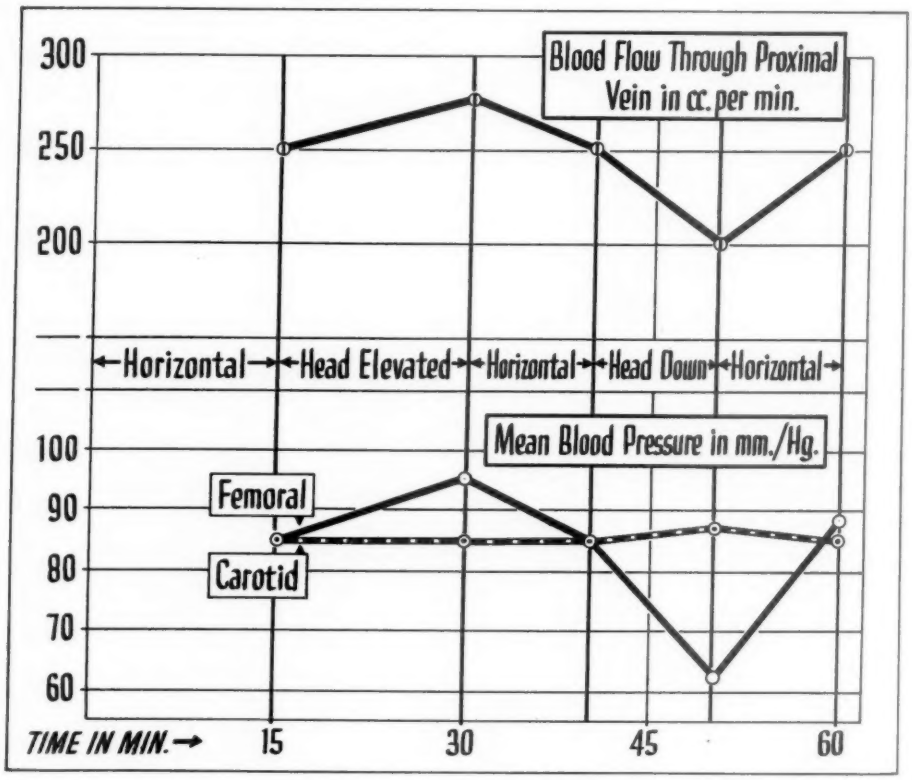

Fig. 2.—Chart showing alterations in blood flow through the proximal vein and in femoral blood pressure with change of position of Dog. 2. Mean carotid pressure was kept at a constant level.

TABLE II. RELATIONSHIP OF FEMORAL AND CAROTID ARTERIAL PRESSURE TO CHANGE OF POSITION

NUMBER OF ANIMAL	CAROTID PRESSURE	FEMORAL PRESSURE		
		HORIZONTAL POSITION	HEAD ELEVATED	HEAD DEPENDENT
2	85	86	100	65
4	150	150		114
	120	118	144	
5	142	138	151	115
	113	112	125	110
6	85	70	96	41
8	154	130		99
9	142	139	151	115
	113	112	125	100

after this procedure. In one, a slight increase in blood flow occurred, in the other no change. The flow through the vein increased in volume from 300 to 425 c.c. per minute immediately after ligation of the distal vein in Dog 5.

DISCUSSION

These studies demonstrate that the blood flow returned directly toward the heart though the proximal vein tends to be considerably greater when the fistula is below rather than above the level of the heart. They do not provide a conclusive answer as to why these differences in volume flow occur. In other studies we have repeatedly shown that with the animal in the horizontal position, the pressure in the femoral vein, equal to arterial pressure at the point where it communicates with the fistula, rapidly decreases in a proximal direction and reaches normal values in the lower vena cava. In these studies, the few observations made indicate that the differences in vena caval pressure with change in position are not as great as are the changes in femoral arterial pressure. Since the velocity of blood flow of a given liquid, and consequently the volume flow, is proportional to the pressure gradient, provided the cross-sectional area of the tube is constant, one might feel that these observed differences provide a possible explanation, and indeed, they may. We have no data, however, permitting us to evaluate other possible related factors such as the differences in force required to move the column of vena caval blood upward against gravity or downward with gravity, or differences in the sucking action of inspiration with the animal in various positions.

Even though the full and precise explanation is not at hand, the experiments reported do demonstrate without question that the volume flow of blood through the proximal vein is greater when the fistula is below heart level than when it is above. These experiments thus provide a satisfactory basis for the clinical observation that fistulas caudad to the heart tend to produce early significant cardiac enlargement much more readily than do fistulas situated cephalad to the heart, in view of the following considerations: The increase in cardiac output in cases of arteriovenous fistula is, as far as we know, directly related to the volume of blood shunted through the fistula directly back to the heart. The cardiac dilatation and hypertrophy which occur in cases of arteriovenous fistula are, as far as we know, directly the result of the increased work load of the heart. During all hours of the day except when the patient is recumbent, fistulas caudad to the heart are below, and those cephalad to the heart are elevated above, heart level.

REFERENCE

1. Shumacker, H. B., Jr., and Stahl, N. M.: A Study of the Cardiac Frontal Area in Patients With Arteriovenous Fistulas, SURGERY 26: 928-943, 1949.

THE USE OF TEMPORARY POLYTHENE SHUNTS TO PERMIT OCCLUSION, RESECTION, AND FROZEN HOMOLOGOUS GRAFT REPLACEMENT OF VITAL VESSEL SEGMENTS

A Laboratory and Clinical Study

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NOT infrequently operative therapy for a wide variety of diseases affecting vital blood vessels is either not considered feasible; or, if proposed, is rejected as impracticable; or, if attempted, is abandoned as prolonged vessel occlusion or sacrifice is encountered. It is not our purpose to review the countless ingenious experiments which attest the interest that has long centered on this challenge.[1-6] Instead we wish simply to report our experience with a method which, though imperfect, appears to have promise.

Two observations form the basis for this experiment: first, the demonstrated practicability of homologous artery preservation and transplantation[7-18]; and, second, the unhurried, accurate procedures which are now regularly employed in isolated aortic segments of patients with aortic coarctation and its attendant collateral circulation.[19-22] In the absence of such a collateral circulation many patent vital arteries cannot be safely occluded long enough to permit careful dissection and grafting.[23-25] Thus it appeared that an artificial temporary arterial shunt must be employed.

Like Clatworthy and Varco we have used Polythene tubing for this purpose.[26] The exact dimensions of the shunt required to maintain adequate minute-volume flow and pressure will be the subject of another report. In general we have employed a shunt to artery ratio of approximately 1 to 7. The number of shunts and their length, of course, depend on the configuration of the vessels to be occluded. The Polythene tubing may be inserted into an artery in diverse ways; however, we have had best results with the following technique: First the tube is cut to proper length so that it curves well out of the operative field. The ends are then flanged by rotating the tube in an alcohol flame, after which the flange is manually molded in hot water so that it has the alignment and curvature of the vessel into which it is to be inserted. Two 000000 sutures are placed transversely in the presenting wall of the vessel proximal and distal to the point chosen for insertion. A longitudinal stab incision is made in the vessel between the sutures, the flanged end of the shunt is inserted into the defect, the ligatures tied, and the tubing withdrawn until the flange engages the vessel wall. A clamp is placed on the tube during insertion. With the proximal end in place this clamp is released and the shunt is allowed to fill with blood. The distal end of the shunt is placed, after which the clamp is again removed. The vessel then may be safely crossed-clamped for an indefinite period.

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Prerequisite for this project has been the development of an artery bank. Dog vessels have been easily obtained from our kennel population. Human vessel procurement, however, poses such difficulties that at times the continuation of the entire project has been threatened. Some of these problems will be set forth in a subsequent report. As to strictly technical considerations we have proceeded as follows: With standard aseptic precautions the aorta and all of its branches are resected in one specimen from the heart through to and including the external and internal iliac arteries. This specimen is then divided into several sections: (1) the ascending, transverse, and first part of the descending thoracic aorta with long lengths of the innominate, left common carotid, and subclavian arteries attached; (2) most of the remaining descending thoracic aorta; (3) the lower descending thoracic aorta and the upper abdominal aorta with the celiac axis and its branches and the superior mesenteric artery attached; (4) the remaining abdominal aorta with the renal and common iliac arteries attached; and (5) short lengths of smaller vessels such as the external iliac, internal iliac, femoral, subclavian, and carotid arteries, etc., which are packaged separately. These specimens are individually wrapped in saline-soaked gauze and are placed in stainless steel containers which are then immersed in a mixture of ethyl ether and solid CO_2. After quick freezing to –72° C. the grafts are then stored in a deep freeze at –40° C. They are made ready for use by thawing in warm normal salt solution.

TABLE I. AORTIC GRAFT WITHOUT SHUNT

DOG NO.	WEIGHT (IN KG.)	TIME AORTA CROSS-CLAMPED (IN MIN.)	COMPLICATIONS	LENGTH OF LIFE AFTER OPERATION	FATE OF ANIMAL	CONDITION OF GRAFT	TIME GRAFT PRESERVED (IN DAYS)
74	11.7	28	Shock	1 hr.	Died	------	30
57	11.2	35	Shock	10 hr.	Died	------	50
99	9.0	29	Shock	45 min.	Died	------	5
145	14.1	25	Shock	1 hr.	Died	------	18
115	11.2	32	Shock	2 hr.	Died	------	30
96	8.2	29	Shock	8 hr.	Died	------	30
73	16.8	30	Spastic paralysis	19 days	Died—distemper	Good—small thrombus at proximal suture	35
101	12.1	30	Spastic paralysis	7 days	Sacrificed	Good—small thrombus at proximal suture	25
11	14.4	27	Spastic paralysis	15 days	Sacrificed	Excellent	30
55	11.5	25	None	35 days	Sacrificed	Excellent	40
105	10.1	40	Spastic paralysis	20 days	Sacrificed	Excellent	20
98	11.0	50	Spastic paralysis	24 days	Sacrificed	Excellent	30
113	8.9	30	Spastic paralysis	30 days	Sacrificed	Excellent	40

Our first observations (Table I) concern 13 mongrel dogs which, without shunting, underwent cross-clamping, resection, and homologous graft replacement of the major part of the descending thoracic aorta. The aorta was ob-

structed in this series for 25 to 50 minutes, with an average of 32 minutes. Six animals died shortly after operation. One of the 7 surviving animals died of distemper 19 days after operation, and the remaining 6 were sacrificed at from 7 to 35 days postoperatively. At autopsy 5 of these 7 survivors presented grafts in excellent condition, while 2 had probably insignificant small mural thrombi at the proximal suture line. All but 1 of these 7 animals had a spastic paralysis of the hind quarters.

TABLE II. AORTIC GRAFT WITH SHUNT

DOG NO.	WEIGHT (IN KG.)	TIME AORTA CROSS-CLAMPED (IN MIN.)	INSIDE DIAMETER OF SHUNT (IN MM.)	DIAMETER OF AORTA (IN MM.)	LENGTH OF LIFE AFTER OPERATION	FATE OF ANIMAL	CONDITION OF GRAFT	TIME GRAFT PRESERVED (IN DAYS)
95	7.5	150	1.57	9	½ hr.	Died—cardiac failure	--------	50
10	8.5	120	1.14	9	6 days	Died—hemorrhage	Infected graft—B. coli	25
50	10.0	50	1.57	11.5	45 days	Sacrificed	Good—small mural thrombus	20
141	16.1	150	2.69	14	130 days	Sacrificed	Good—small mural thrombus	30
12	6.4	45	1.14	85	60 days	Sacrificed	Excellent	12
48	14.2	60	2.15	13.5	100 days	Sacrificed	Excellent	35
54	15.2	165	2.15	14	37 days	Sacrificed	Excellent	55
102	12.6	60	2.69	12	30 days	Sacrificed	Excellent	17
112	15.4	150	2.69	14	150 days	Living	Excellent (aortogram)	7
90	13.8	180	2.15	12	210 days	Living	Excellent (aortogram)	37
114	8.8	105	1.14	10	200 days	Living	Excellent (aortogram)	40

Eleven more mongrel dogs (Table II) were subjected to the same operation except that here Polythene shunts such as described above were employed. The shunts varied in internal diameter from 1.14 to 2.69 mm., depending on the size of the aorta. The aorta was obstructed in this series for from 45 to 180 minutes, with an average of 107 minutes. One dog died shortly after operation in what appeared to be cardiac failure. One dog developed a *Bacillus coli* infection in the operative field and disrupted his graft on the sixth postoperative day. Six of the 9 survivors were sacrificed at from 30 to 130 days postoperatively. Four of these animals presented grafts in excellent condition while 2 had small mural thrombi. The remaining 3 animals were alive and well from 150 to 210 days after operation, and by aortography have been demonstrated to have grafts of normal caliber. None of these animals presented evidence of neurologic disorder. The vessels used in these experiments were stored from 5 to 55 days, with an average of 30 days.

These observations have encouraged us to attempt frozen homologous artery transplantation in 4 patients. In 3, shunts were employed.

CASE 1 (51-1750).—J. M., a 53-year-old white man, was admitted to the Medical Center on Feb. 27, 1951, complaining of severe pain in the lower abdomen and back. These symptoms had been progressive over a three-year period, during which the patient had sought relief by visiting several clinics, each time to be given a fatal prognosis on the basis of a diagnosis of arteriosclerotic aneurysm of the abdominal aorta. He had been bedridden since November, 1950. On physical examination a pulsating mass, 15 cm. in diameter, was found to occupy the midline of the abdomen, centering just below the umbilicus. All of the peripheral vessels felt arteriosclerotic, and the retinal vessels presented A-V nicking and silver wiring. Dorsalis pedis pulses were present. Because of calcification, the aneurysm was clearly demonstrable on x-ray films of the abdomen (Fig. 1). Extensive vertebral erosion

Fig. 1 (Case 1).—Large calcified arteriosclerotic aneurysm of the abdominal aorta. Skeletal views showed marked erosion of vertebral bodies L_2, L_3, L_4, and L_5.

was also seen. On March 2, 1951, under continuous spinal anesthesia, the aneurysm was exposed through a long transverse incision in the anterior abdominal wall. It extended from a point 2 cm. below the renal arteries through and including the iliac bifurcation, and measured 15 by 10 cm. The vena cava was densely adherent to its right posterolateral wall. Two Polythene shunts, each 30 cm. long and 1.67 mm. in diameter, were placed in the aorta at the level of the renal arteries. The distal ends were placed in the common iliac arteries (Fig. 2). The aorta and common iliac arteries were then cross-clamped for 83 minutes during which period the circulation was maintained via the Polythene shunts. During this interval the aneurysm was resected and a 15 cm. segment of homologous aorta bearing common iliac arteries 2 cm. long was sutured in place with continuous 000000 silk (Fig. 3). This graft had been stored for 12 days. Satisfactory iliac suture lines were obtained; however, the

Fig. 2.

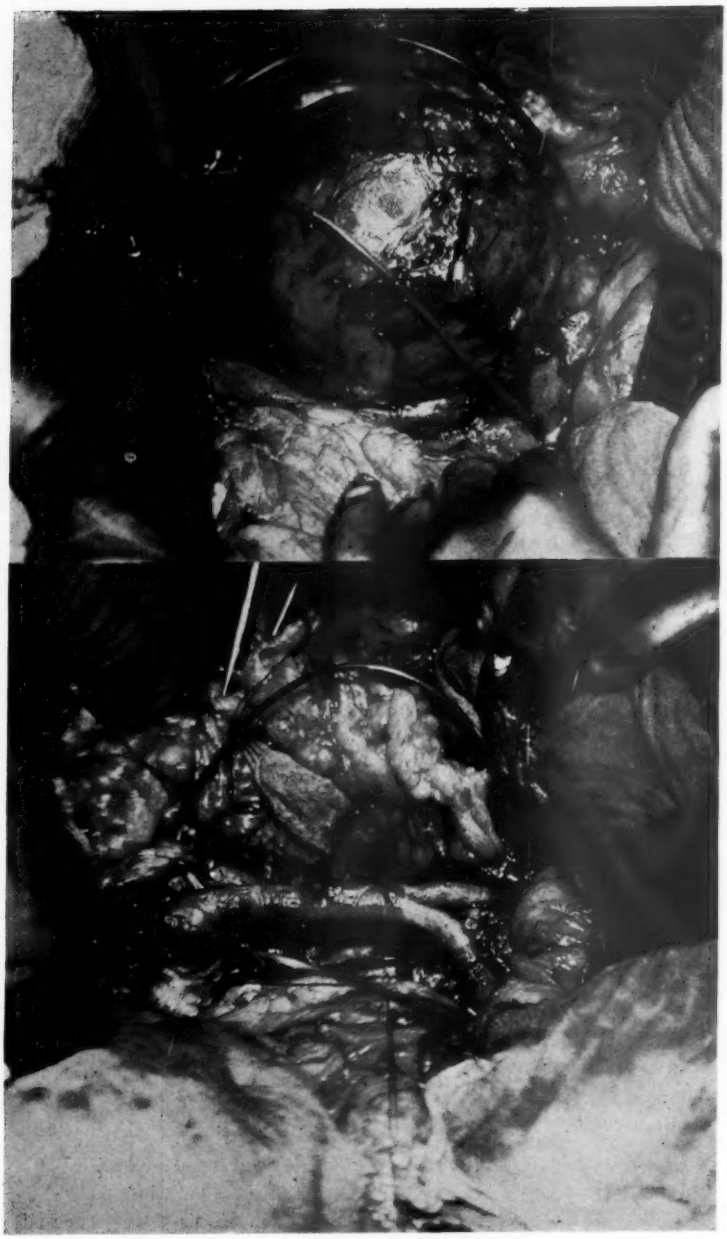
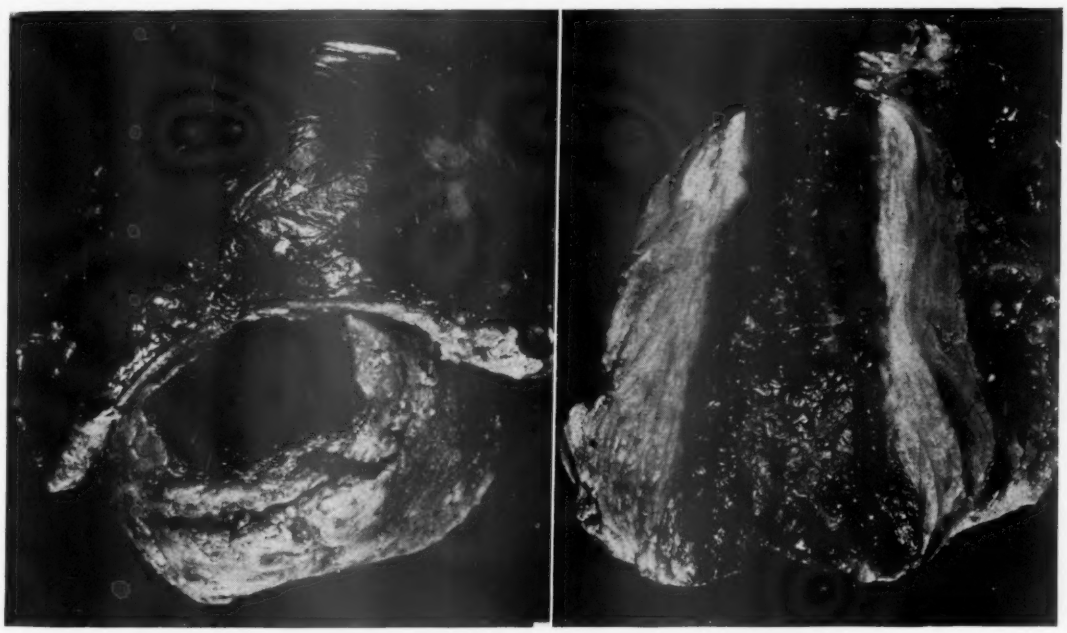


Fig. 3.

Fig. 2 (Case 1).—Appearance of aneurysm at operation. Two Polythene shunts are seen extending from the aorta proximal to the aneurysm to the common iliac arteries distal to their involvement by the aneurysm.

Fig. 3 (Case 1).—Homograft in place. Aortic and iliac clamps have been released but shunts have not yet been removed.

proximal aortic line was worrisome from the beginning, since in this area calcified plaques had to be curetted away before the needle could be made to penetrate the wall. However, no leakage was noted at the conclusion of the operation after the clamps and the shunts had been removed. Dissection of the operative field did not suggest the presence of a collateral circulation of any significance, and gross inspection of the resected specimen revealed the canalized thrombus to have a 2.5 cm. bore (Fig. 4). The patient enjoyed an uneventful early postoperative course, had good dorsalis pedis pulses, no sensory or motor disturbances in the lower extremities, and no urinary or fecal incontinence. He was ambulatory on the fourteenth day and by the twentieth day was symptom free and planned to return home the following morning. That night he experienced sudden pain in the right leg, which became pale from the calf down. He was thought to have had thrombosis of the popliteal artery due to arteriosclerosis, or to have developed a mural thrombus in the graft area with



A. *B.*

Fig. 4 (Case 1).—*A*, Axial, and *B*, longitudinal sectional views of resected aneurysm showing the large bore of its canalized thrombus.

embolization of the popliteal artery. In any event, after paravertebral blocks and anticoagulant therapy the leg appeared much improved and optimism again prevailed. Unfortunately, on the twenty-ninth postoperative day he died suddenly of massive intra-abdominal hemorrhage. At autopsy the graft appeared to be in excellent condition, hemorrhage having occurred through an area of curettage of the host aorta at the proximal suture line. Severe arteriosclerotic changes were seen in all of the remaining abdominal aorta but the arch and descending thoracic aorta were relatively free of disease.

Comment.—We felt that our experience with this patient proved the efficacy of Polythene shunts in maintaining adequate circulation during a prolonged period of aortic occlusion, but that to have been successful our resection and graft replacement should have included the entire abdominal aorta with its celiac, superior mesenteric, and renal branches—a feasible procedure.

CASE 2 (51-25826).—A. B., a 61-year-old white man, was brought to the emergency room of the Medical Center on May 18, 1951, one hour after blasting away the medial aspect of his left upper arm in an unsuccessful suicide attempt with a shotgun. He was in profound shock due to exsanguination and required massive whole blood transfusion and oxygen therapy in preparation for operation which was carried out under Pentothal Sodium, nitrous oxide-oxygen

Fig. 5.

Fig. 6.

Fig. 5 (Case 2).—Appearance of the area of injury 55 days after primary operation.
Fig. 6 (Case 2).—Retrograde arteriogram made on the fiftieth postoperative day. The femoral artery homograft still maintains its large caliber.

anesthesia, two and one-half hours after injury. The left forearm and hand were cold, pale, and pulseless. At operation he was seen to have lost a 15 by 10 cm. area of skin, half of the triceps and biceps muscles, a 10 cm. segment of brachial artery, and a 3 cm. segment of median nerve. The ulnar and radial nerves were intact. All devitalized muscle was excised, the median nerve sutured, and a 10 cm. homologous femoral artery graft sutured into the brachial artery defect. A femoral artery graft was employed since it was the smallest vessel we had in the artery bank. It had been stored for 44 days. The operative

field was covered with a 20 by 15 cm. pedicle flap elevated from the chest wall. This flap was partially detached from the chest wall on the twentieth postoperative day, and its severance completed on the twenty-sixth day. Defatting and final revision were done on the thirty-first day (Fig. 5). Stellate block and anticoagulant therapy were employed during the first week following operation. The patient now had good radial and ulnar pulses with only his median nerve paralysis as a residue. He has been diagnosed as having involutional melancholia and is now undergoing shock therapy in our psychiatric division. By retrograde arteriography the graft appeared to be in excellent condition on his fiftieth postoperative day (Fig. 6).

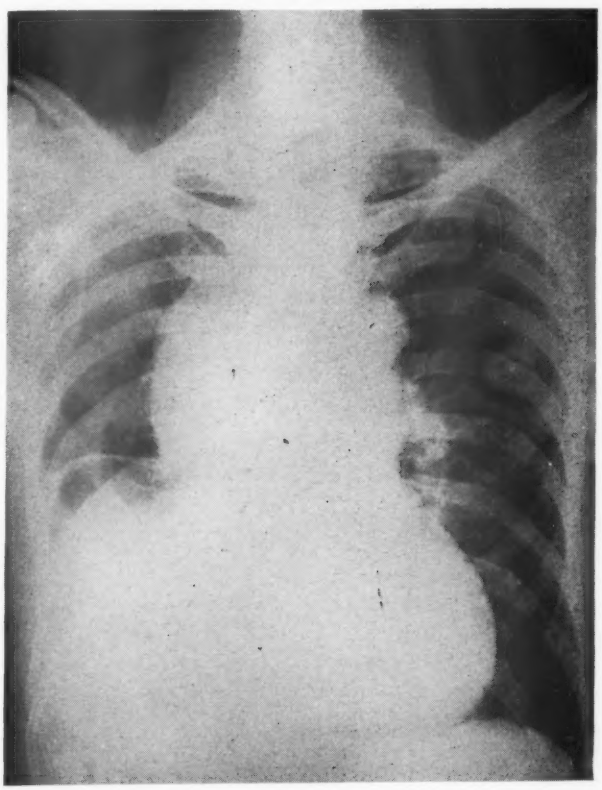


Fig. 7 (Case 3).—Large aneurysm of the ascending aorta with paralysis of the right diaphragm. The right pleural space had by this time been aspirated free of blood.

Comment.—The 44-day-old frozen graft used in this operation was twice as large as it should have been and was placed in a contaminated field, yet apparently has yielded a completely satisfactory result. A shunt was not employed in this patient since it was felt that the ischemic tissues of the forearm and hand would tolerate this insult. If the patient had not reached the hospital so quickly, or if he had not been prepared for operation so promptly, a shunt would have been used, if necessary as part of his emergency management.

Case 3 (51-3444).—C. J., a 60-year-old Negro man, experienced rupture of a syphilitic aneurysm of the aortic arch into the right pleural space three weeks prior to his admission to the Medical Center. This had been managed by repeated thoracentesis and massive transfusion therapy by his local physician and at the Veterans Administration Hospital, Wadsworth, Kan.,

Fig. 8.

Fig. 9.

Fig. 8 (Case 3).—Appearance of operative field after resection of the ascending aorta, arch, and upper descending aorta. In this view all vessels are cross-clamped and one large and three small shunts are functioning. The trachea and superior vena cava are seen in the depths of the wound.

Fig. 9 (Case 3).—Homograft in place. All clamps have been released but shunts have not yet been removed.

from which institution he was transferred to the Medical Center. On physical examination he appeared to have only a moderate aortic regurgitation. The Kahn test was positive. X-ray examination of his chest revealed a calcified aneurysm of the ascending aorta measuring approximately 10 by 8 cm. (Fig. 7). The right diaphragm was paralyzed. Bleeding from the aneurysm appeared to have stopped. On April 27, 1951, under Baird's solution, nitrous oxide-oxygen anesthesia, his chest was opened through a transverse incision which extended into each axilla. This incision followed the line of the left third and right second intercostal spaces. The sternum was cut transversely and its proximal fragment split longitudinally. The pericardium was widely incised and the base of the heart together with the aorta and

Fig. 10 (Case 4).—Calcified arteriovenous aneurysm of the abdominal aorta and inferior vena cava.

all of its branches exposed. The pulsating aneurysm occupied the distal ascending aorta and extended into the right side of the arch. The superior vena cava was firmly adherent to its right posterolateral wall. Four Polythene shunts, each 20 cm. long, were placed in the aorta just distal to the aortic valve. Three of these, each 2.9 mm. in diameter, were connected to the innominate, left common carotid, and left subclavian arteries respectively. The fourth, measuring 9.52 mm. in diameter, was inserted into the descending thoracic aorta. Just after placement of these shunts, but before any cross-clamping had begun, the heart began to fibrillate, and in spite of all our efforts, which included the intravenous administration of Pronestyl and procaine, manual massage, and electric shock, this rhythm persisted. The ascending aorta, the innominate, left common carotid, and left subclavian arteries, and the descending thoracic aorta were cross-clamped and transected; and most of the ascending

Fig. 11.

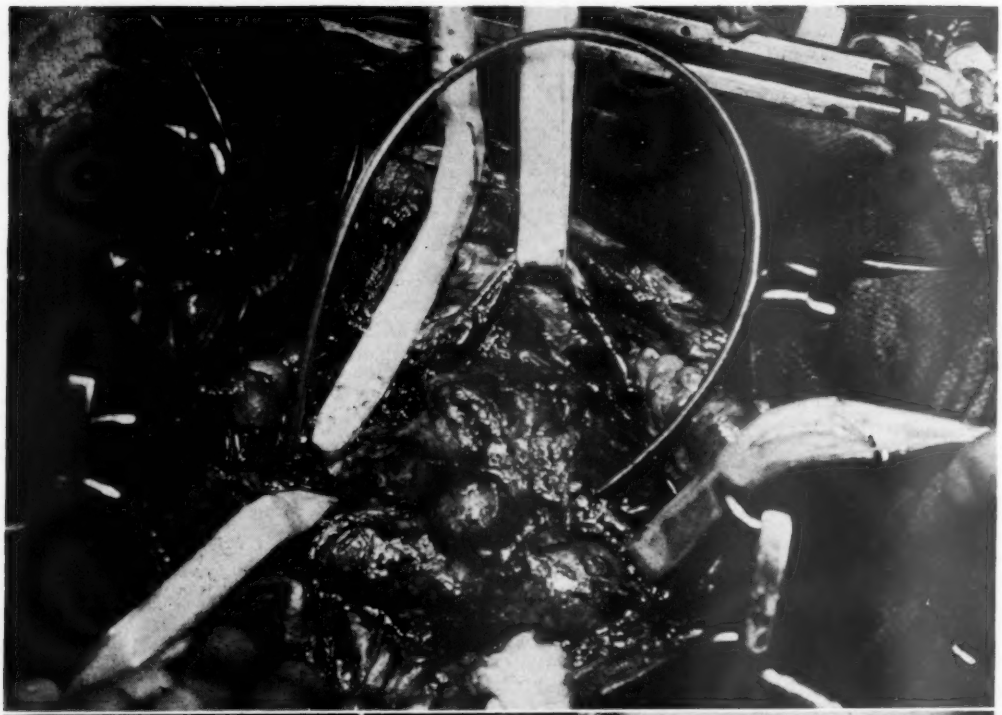


Fig. 12.

Fig. 11 (Case 4).—Appearance of operative field showing the arteriovenous aneurysm between the tremendously dilated aorta and vena cava. One 2.15 mm. shunt has been placed in the aorta around the aneurysm.

Fig. 12 (Case 4).—Homograft in place. Clamps and shunt have been removed.

aorta, the entire arch, and the upper descending aorta with all of the arch branches were then resected (Fig. 8). A 30-day-old frozen graft was then sutured into position and the clamps and shunts removed (Fig. 9). The duration of occlusion was 150 minutes. The patient's fibrillation continued after operation and he finally died one hour postoperatively.

Comment.—Technically this was the easiest of the 4 operations included in this report. We are still at a loss to explain the development of this vicious cardiac arrhythmia. Perhaps it relates to the operative procedure itself, or possibly such a reaction should not have been surprising in view of the severe arteriosclerosis this 60-year-old syphilitic man presented.

Fig. 13 (Case 4).—Retrograde aortogram made on the fiftieth postoperative day. The graft maintains its large caliber.

CASE 4 (51-26054).—C. DeL., a 20-year-old white man, accidentally sustained a 22-caliber-gunshot wound of the abdomen three years before admission to the Medical Center. He had been explored at the time of injury but the operation was abandoned as a large retroperitoneal hematoma was encountered. He had been rejected for military service in 1950 when an x-ray film of his chest revealed that his heart was markedly enlarged. Physical examination revealed the presence of a pulsating mass, 5 cm. in diameter, in the midline of the abdomen just below the umbilicus. A thrill and harsh bruit were present in this area, and the latter was transmitted to almost all parts of the body, being clearly audible on auscultation of the skull or at the base of the spine. The blood pressure obtained in his right arm was 155/40 mm. Hg. A positive Branham's sign could be elicited as pressure was exerted on the abdominal mass. X-ray films of the abdomen revealed the mass to be calcified (Fig. 10). A diagnosis of arteriovenous aneurysm with large bore communication between the abdominal aorta and inferior vena cava was made. On June 8, 1951, under continuous spinal anesthesia, the abdomen was explored through a transverse incision. The aneurysm,

measuring 5 cm. in diameter, was found to involve the aortic wall from a point 5 cm. distal to the renal arteries to within 1 cm. of the aortic bifurcation. A Polythene shunt, 15 cm. long and 2.15 mm. in diameter, was inserted into the aorta above and below these points (Fig. 11). The inferior vena cava was partially occluded with a large Potts clamp, and the aorta was clamped above and below the aneurysm, which was then resected together with a 10 cm. segment of aorta. The resultant defect in the vena cava was simply closed with a continuous suture of 000000 silk. A 50-day-old frozen homologous aortic graft was sutured into the defect in the aorta. Clamps and shunts were removed (Fig. 12). Postoperatively, the patient was placed on anticoagulant therapy but this was discontinued after four days because so much oozing of blood had occurred into the operative field. On the seventh postoperative day the abdomen was reopened and this large hematoma extracted. The graft at this time appeared to be in excellent condition and the suture lines were dry. Anticoagulant therapy was not begun again and no further bleeding occurred. Aside from mild transient edema of the feet and ankles, due apparently to partial caval obstruction at operation, no other untoward complications followed. The patient experienced early, marked reduction in heart size. On the fiftieth day after operation, a catheter was threaded up the aorta from the right femoral artery and the aortogram made by this technique revealed the graft to be of excellent caliber (Fig. 13).

Comment.—This patient appears to have had an excellent result marred only by bleeding as the result of anticoagulant therapy. We plan not to subject subsequent patients to this hazard.

SUMMARY

In both human beings and dogs it appears feasible to maintain adequate circulation via Polythene shunts during temporary occlusion of the aorta, thus permitting homologous graft replacement of resected aortic segments. Though not necessarily best for this purpose, frozen grafts appear to have yielded satisfactory results. This technique should be applicable to the management of a wide variety of diseases affecting vital vessels. We have listed our failures and successes with the method.

REFERENCES

1. Carrel, A.: Permanent Intubation of the Thoracic Aorta, J. Exper. Med. **16**: 17, 1924.
2. Blakemore, A. H., and Lord, J. W.: A Non-suture Method of Blood Vessel Anastomosis, Ann. Surg. **121**: 435, 1945.
3. Hufnagel, C. A.: Permanent Intubation of the Thoracic Aorta, Arch. Surg. **54**: 382, 1947.
4. DeCamp, P. T., Spencer, R., and Overstreet, J. W.: Experimental Studies in Delayed Homologous Arterial Grafting Utilizing an Intra-arterial Shunt, Surgical Forum, Proc. Thirty-sixth Clin. Cong. A.C.S., 1950, Philadelphia, 1951, W. B. Saunders Company, p. 282.
5. Smith, S.: A Soluble Rod as an Aid to Vascular Surgery, Arch Surg. **41**: 1004, 1940.
6. Shumacker, H. B., Jr.: The Problem of Maintaining the Continuity of the Artery in the Surgery of Aneurysms and Arterio-venous Fistulae, Ann. Surg. **127**: 207, 1948.
7. Guthrie, C. C.: End Results of Arterial Restitution With Devitalized Tissue, J. A. M. A. **73**: 186, 1919.
8. Levin, I., and Larhin, J. H.: Transplantation of Devitalized Arterial Segments, Proc. Soc. Exper. Biol. & Med. **5**: 109, 1907-1908.
9. Carrel, A.: Latent Life of Arteries, J. Exper. Med. **12**: 460, 1910.
10. Carrel, A.: Heterotransplantation of Blood Vessels Preserved in Cold Storage, J. Exper. Med. **9**: 226, 1907.
11. Shumacker, H. B., Jr., Freeman, L. W., Wayson, E. E., and Stahl, H. H.: Studies in Vascular Repair, The Yale J. Biol. & Med. **23**: 81, 1950.
12. Deterling, R. A., Jr., Coleman, C. C., and Parshley, M. S.: Experimental Studies of the Frozen Homologous Aortic Graft, SURGERY **29**: 419, 1951.
13. Eastcott, H. G., and Hufnagel, C. A.: Preservation of Arterial Grafts by Freezing, Surgical Forum, Proc. Thirty-sixth Clin. Cong., A.C.S., 1950, Philadelphia, 1951, W. B. Saunders Company, p. 269.

14. Peirce, E. C., Gross, R. E., Bill, A. H., and Merrill, K.: Tissue Culture Evaluation of the Viability of Blood Vessels Stored by Refrigeration, Ann. Surg. **129**: 333, 1949.
15. Gross, R. E., Bill, A. H., Jr., and Peirce, E. C., II: Methods for Preservation and Transplantation of Arterial Grafts, Surg., Gynec. & Obst. **88**: 689, 1949.
16. Swan, H., Robertson, H. T., and Johnson, M. E.: Arterial Homografts. I. The Fate of Preserved Aortic Grafts in the Dog, Surg., Gynec. & Obst. **90**: 568, 1950.
17. Swan, H., Maashe, C., Johnson, M., and Grover, R.: Arterial Homografts. II. Resection of Thoracic Aortic Aneurysm Using a Stored Arterial Transplant, Arch. Surg. **61**: 732, 1950.
18. Swan, H., and Morfit, H. M.: Arterial Homografts. III. Use of Preserved Grafts in the Treatment of Neoplastic Disease Involving Peripheral Arteries, Arch. Surg. **62**: 767, 1951.
19. Crafoord, C. G., Ejrup, B., and Gladnikoff, H. H.: Coarctation of Aorta, Thorax **2**: 121, 1947.
20. Gross, R. E., and Hufnagel, C. A.: Coarctation of Aorta. New England J. Med. **233**: 287, 1945.
21. Blalock, A., and Park, E. A.: The Surgical Treatment of Experimental Coarctation (Atresia) of the Aorta, Ann. Surg. **119**: 445, 1944.
22. Bing, R. J., Handelsman, J. C., Campbell, J. A., Griswold, H. E., and Blalock, A.: The Surgical Treatment and the Physiopathology of Coarctation of the Aorta, Ann. Surg. **128**: 803, 1948.
23. Mann, F. C., Herrick, J. F., Essex, H. E., and Blades, E. J.: Effects on Blood Flow of Decreasing Lumen of Blood Vessels, SURGERY **4**: 249, 1938.
24. Shorr, E., Zweifach, B. W., and Furchgott, R. F.: On the Occurrence, Sites and Modes of Origin and Destruction of Principles Affecting the Compensating Vascular Mechanisms in Experimental Shock, Science **102**: 489, 1945.
25. Frank, H. A., Seligman, A. M., and Fine, J.: On the Specific Role of the Liver in Hemorrhagic Shock, Ann. Surg. **126**: 1002, 1947.
26. Clatworthy, H. W., and Varco, R. L.: A Small Bore Polythene Shunt to Prevent Mechanical Shock After Prolonged Cross-clamping of the Thoracic Aorta, Proc. Soc. Exper. Biol. & Med. **74**: 434, 1950.

A NEW INJECTION DEVICE FOR ANGIOGRAPHY

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THIS report is a description of a simple device, suitable for all forms of angiography, which enables the user to vary and control the amount, rate, and force of injections of contrast material; and which controls the switch of the x-ray machine. If desired, that control can be extended to the operation of a cassette changer. It lends itself to aseptic technique. Its design permits further adaptation to control by electric impulses, such as those of cardiac origin. The latter has been omitted from the present model.

During studies of experimental coronary artery occlusion by means of coronary angiography (Pearl and associates) it became apparent that more precision was necessary than that obtained by usual manual methods of injecting the contrast medium, and timing the injection of the contrast material. The manual techniques often are successful, but the successes are sporadic, and the factors are not measurable. The variations in the rate and the forcefulness of injection by hand are not easily controlled, especially when the volume of the contrast material is small. Furthermore, the rate of injection and the timing of the roentgenogram is a most particular problem in coronary arteriography where the interval of one or two heart beats must include both the injection and the exposure. Another undesirable element of the manual method is the danger from broken syringes in the hands of the injector.

The accompanying photographs illustrate the features of the apparatus. It is a cylindrical metal shell which houses a Robb type Luer-Lok glass syringe, and a compression chamber, which is fed by a tank of nitrogen gas. This was developed from the devices of dos Santos, Nelson, Doss, and Fariñas. It has the added safety factor of metal stops which permit the injection of any desired amount of contrast material. Further safety is obtained by fitting the plunger of the compression chamber to the plunger of the syringe in such a way that the latter cannot reach the bottom of the syringe barrel (lacking 5 ml. in the 20 ml. syringe, and 10 ml. in the 50 ml. syringe). Although this wastes some of the contrast medium, the shattering of the syringe by abutment of piston against barrel is prevented.

Double control is obtained by stopcocks at the ends of the cylinder. One three-way stopcock is attached to the distal end of the syringe. This is connected to a supply of heparinized isotonic solution, and to the intravascular catheter. The latter opening may be used for filling the syringe with radiopaque solution for the angiogram. A second stopcock is placed at the proximal end where the compressed nitrogen enters the cylinder. By adjusting

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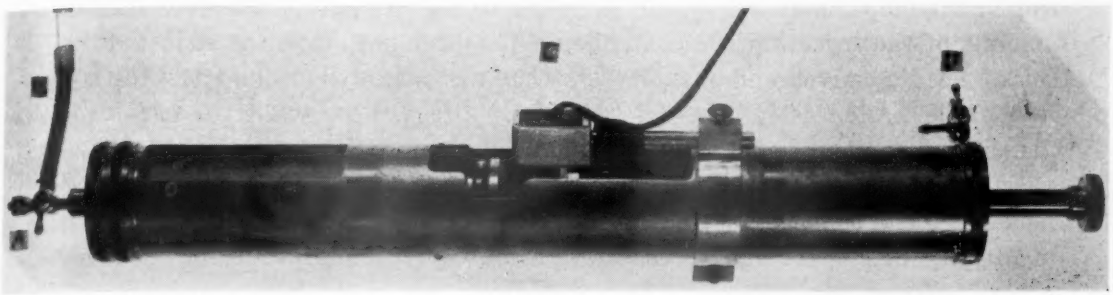

Fig. 1.—The assembled injector. *A*, Three-way stopcock at syringe end. The Luer-Lok attachment fits the intravascular catheter. *B*, Tubing connected to pressure bottle containing heparinized solution. *C*, Microswitch on adjustable rod. Wire leads to relays that control the x-ray machine. *D*, Three-way stopcock at end of compression chamber. One opening is connected to a tank of compressed nitrogen. The other is an exhaust valve to release the piston when the injection is completed.

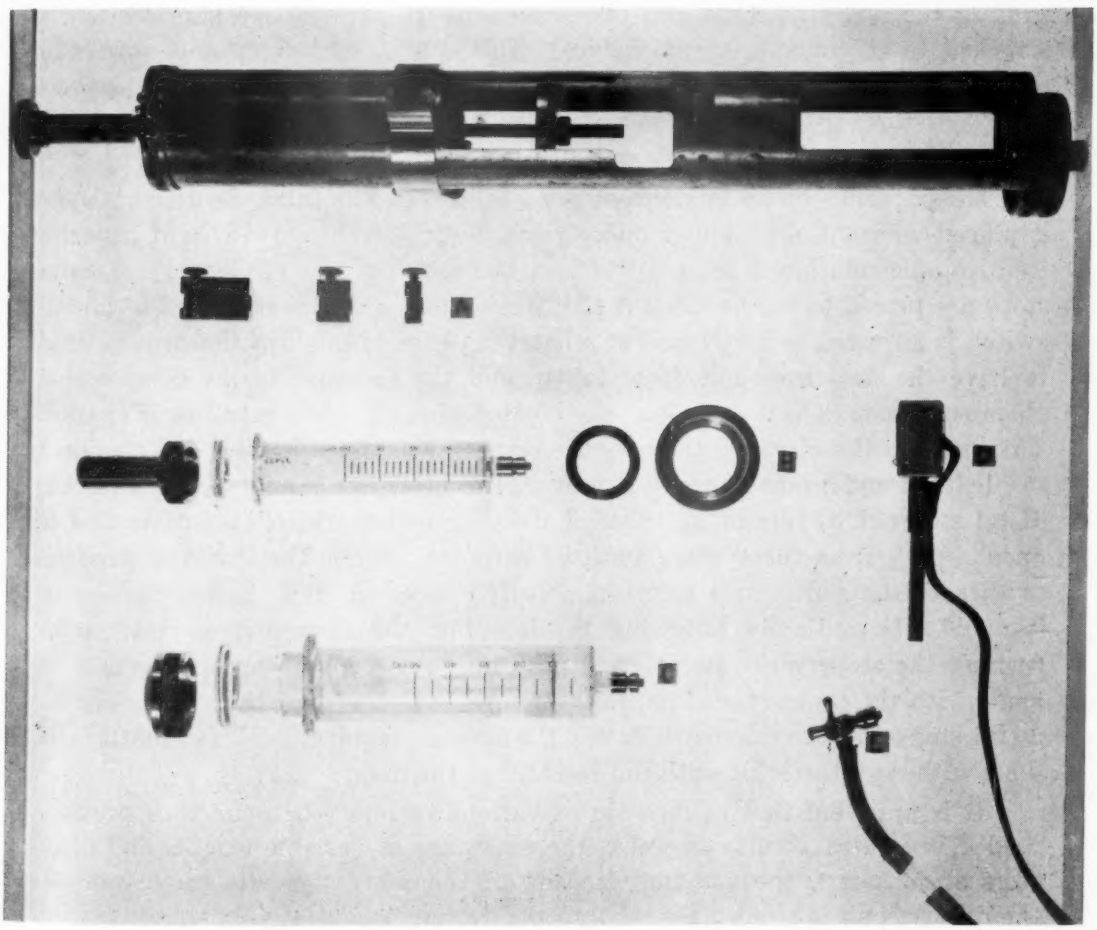

Fig. 2.—The parts. The device is easily dismantled. The metallic outer cylinder is above. The compression piston may be removed from the chamber by unscrewing the cap at upper left. The syringes and their fittings are removed by unscrewing the cap at upper right. *A*, Metal stops that attach to the piston handle seen extending from the cylinder at upper left. These correspond to 5, 10, and 20 ml. graduations on the 50 ml. syringe. *B*, 20 ml. syringe and adaptive fittings. *C*, 50 ml. syringe. The fittings for the plunger trips the microswitch. *D*, The fine wire on the under surface of the switch is touched by the fitting as it passes by during the injection. *E*, Three-way stopcock connecting syringe, intravascular catheter, and heparinized solution.

the metal stops, and fixing the pressure of the injection, the rate and the amount of the injection are controlled. The pressure system is adjusted by a set of needle valves and manometers that are mounted around the top of a table. The system is connected to a tank of nitrogen gas which feeds the compression chamber of the injector, and provides a force for a constant intravascular drip to keep the catheter clear of clots between injections of contrast medium. The solution for the constant drip flows from a pressure bottle with a Murphy drip attachment. There is a blow-off path through an adjustable column of mercury to prevent excessive pressures in the bottle, and excessive injection of fluid. This is of particular value when the room is darkened to permit the use of the fluoroscope, because the rate of the drip cannot then be observed, and a means of avoiding injecting too much fluid must be provided.

This apparatus differs from other pressure injectors in its method of controlling the x-ray machine and cassette changer. A sensitive microswitch is attached to the outside of the device. This can be moved up and down the length of the cylinder. It is tripped by the plunger of the syringe as it passes by. Therefore, its position along the cylinder permits the taking of the roentgenogram after any desired amount of injection of radiopaque medium.

The sequence of an angiogram is as follows: The intravascular catheter is placed where desired under fluoroscopic control. The slow drip of heparinized isotonic solution is adjusted to keep the catheter free of clots. The metal stops are placed to fix the amount of injection of contrast medium. The microswitch is adjusted to be tripped at whatever phase of the injection it is desired to have the first roentgenogram taken, and the pressure to the compression chamber is set. The stopcock at the compression chamber entrance is opened. This permits the nitrogen to enter the compression chamber and drive against the leather and brass piston. However, the injection cannot occur until the distal stopcock is turned, to shut off the drip of heparinized solution, and to open a path from the syringe into the catheter. When the distal stopcock is so turned, the radiopaque solution is swiftly injected, and the roentgenogram is made. Immediately following the injection the slow drip is restored by turning the stopcock to its original position. Succeeding angiograms may be made with the contrast medium that remains in the syringe, by readjusting the metal stops and the microswitch. If the syringe requires refilling, that can be done without interfering with the catheter or the drip.

It is apparent that calibration of various factors (the pounds of pressure needed, the intravascular pressure, the resistance of variable lengths and diameters of catheters, the varying viscosity of the contrast media employed, and the different sizes of syringes set into the device) is a relatively simple matter. The viscosity, syringe, and length-of-catheter factors are of minor importance. On the other hand, the intravascular pressure against which the injection must be made, and the lumen of the catheter are the important factors against which the pressure of injection must be calibrated. For instance, we have found that forty pounds per square inch of pressure in the compression chamber delivered

through a 50 ml. syringe will inject 5 ml. of 70 per cent Diodrast in about one second through an 80 cm. woven silk catheter into the ascending aorta of a dog, where the systolic pressure is around 120 mm. Hg.

The insertion of an electrically controlled valve into the outflow path would permit the control of the injection by electrocardiac impulses. This would extend the usefulness of the device beyond its present capacities, without changing its basic design.

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REFERENCES

Pearl, F. L., Friedman, M., Gray, N., and Friedman, B.: Coronary Arteriography in the Intact Dog, Circulation, **1**: 1188, 1950.

Pearl, F. L., Gray, N., and Friedman, B.: Retrograde Aortography With a Special Catheter Including Demonstration of the Coronary Arteries, Ann. Surg. **132**: 659, 1950.

dos Santos, R., Lamas, C., and Caldas, P.: Les récents progrès dans la technique de l'artériographie de l'aorte abdominale, Presse méd. **39**: 574, 1931.

Doss, A. K.: Translumbar Aortography—An Apparatus for Injecting the Radiopaque Media, SURGERY **16**: 422, 1944.

Fariñas, P. L.: Retrograde Arteriography of the Abdominal Aorta and Iliac Arteries, SURGERY **18**: 244, 1945.

Nelson, O. A.: Arteriography of Abdominal Organs by Aortic Injection, Surg., Gynec. & Obst. **74**: 655, 1942.

DOUBLE AORTIC ARCH

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DOUBLE aortic arch is a congenital malformation in which both the right and left fourth branchial arches persist. Usually the right fourth primitive arch disappears during embryologic development, and the left persists to form the normal left-sided arch. This is situated in front of the trachea and esophagus. The left fourth arch also may disappear during development leaving the right arch as the definitive structure. It usually ascends on the right, passes posteriorly to the trachea and esophagus, and is continued down the left thorax as the descending aorta. There also may be rare instances in which the right arch passes in front of, rather than behind, the trachea and esophagus.

When both the right and left primitive fourth arches persist, there develops a double structure, one limb of which passes anteriorly to the trachea and esophagus, the other passes posteriorly to these structures. They join distally and are continued downward as the descending aorta. The trachea and esophagus are, therefore, encircled by a ring of vascular tissue.

Although the possible surgical significance had been pointed out previously by Sprague and associates,[1] Gross,[2] in 1945, was the first to divide one of these structures. Since that time Sweet, Findlay, and Reyersbach,[3] Gross and Ware,[4] Potts and associates,[5] Bahnson and Blalock,[6] and others have reported surgical corrections of this anomaly. In addition to the double arch there are other types of constricting vascular lesions, such as the anomalous right subclavian artery which passes posteriorly to the esophagus to reach the right arm, and the right arch with a ductus arteriosus or its remnant, the ligamentum arteriosum, which holds the pulmonary artery against the trachea. This manuscript deals only with the double arch. The double arch may be the only anomaly present or it may occur in conjunction with other cardiac lesions. Bahnson and Blalock[6] reported double arches in patients with tetralogy of Fallot, and I have encountered one such case. The double arch was not producing symptoms, but the posterior or small arch was divided because it was the origin of the left subclavian artery and dividing it added length to the artery.

Griswold and Young[7] reviewed the literature in 1949. They found forty-seven reported cases of double aortic arch up to that time, although there was some question as to the exact anomaly in some of these cases. Five patients had been operated upon; two of these succumbed and three survived. Undoubtedly other patients have been operated upon and have not been reported in the literature to date.

The two limbs of the arch compress the trachea and esophagus, and the symptoms produced therefrom are those of tracheal and esophageal obstruction. These consist of wheezing respiration, cough, dyspnea, and varying degrees of

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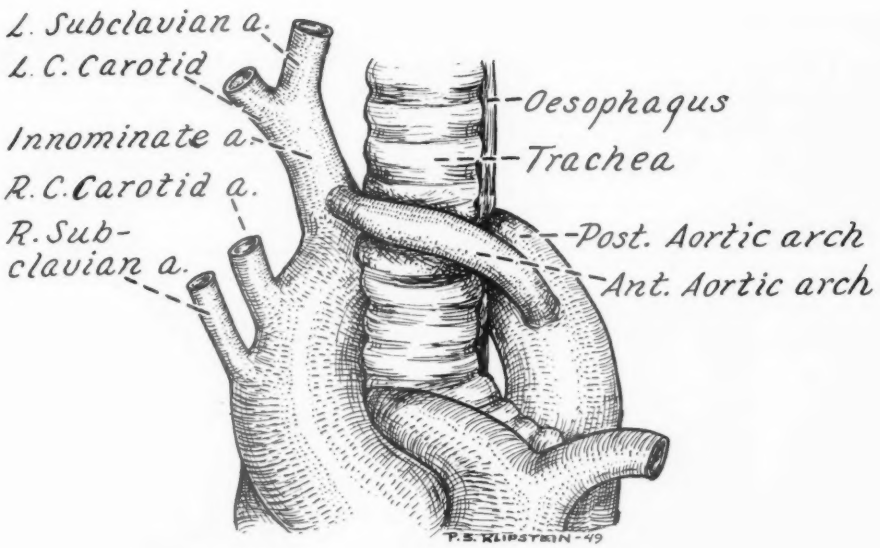

Fig. 1.—Diagram of type of double arch in Case 1.

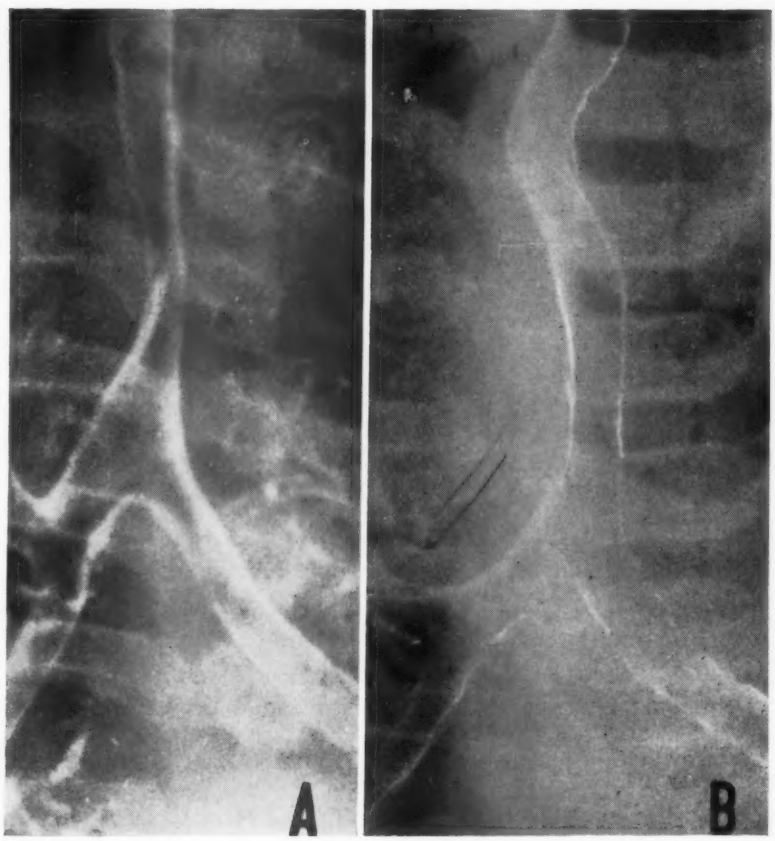

Fig. 2.—Tracheograms of first patient (*A*) before operation and (*B*) two weeks postoperatively. (*B* retouched.)

tracheobroncho-pulmonary infection. The symptoms usually appear soon after birth and are markedly aggravated by the first respiratory infection, especially in those patients with severe constrictions. Since the esophagus is partially obstructed, there may be dysphagia, and aspiration of food, especially in the infant. The double aortic arch does not always produce symptoms, as it is sometimes found at necropsy in an older patient who has had no known symptoms of this anomaly. The degree of tracheal or esophageal constriction, rather than the mere presence of the double arch, determines the symptoms.

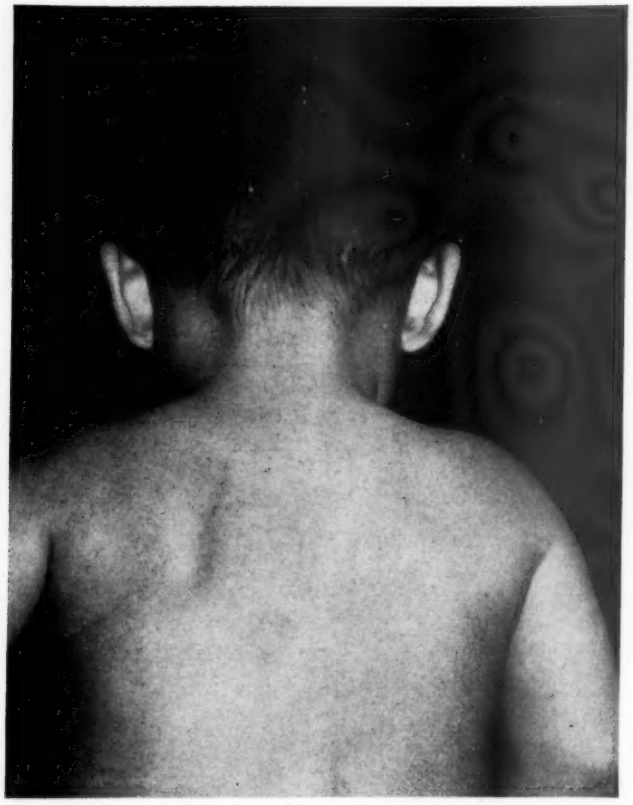

Fig. 3.—Patient in Case 1, one year postoperatively.

The diagnosis is not difficult to make, provided the anomaly is producing an appreciable constriction. The compression of the esophagus is readily seen with the barium swallow. The tracheal constriction may be seen in the lateral roentgenogram of the thorax, and can be visualized more plainly if a small amount of Lipiodol is injected into the trachea before the roentgenograms are made. Angiocardiograms do not seem warranted in the average patient. The tracheal narrowing is easily seen through the bronchoscope.

The relief of the constricting symptoms is obtained by the division of one of the arches and the complete dissection of the vascular structures from the trachea and esophagus. Since the trachea of the young child is less rigid than that of the older patient, operation should be carried out as soon as feasible.

CASE REPORTS

CASE 1.—An 8-month-old boy was first seen during the period of acute tracheobronchopulmonary suppuration. There were atelectasis of the right upper lobe, marked dyspnea, a loud tracheal rattle, and a fever of 103° F. This child had been in the hospital all his life except for about two weeks at home. Aside from the tracheobroncho-pulmonary pathology the child seemed normal. The heart was of normal size, there were no murmurs, and the electrocardiogram showed no abnormalities. The blood count showed a marked leucocytosis but was otherwise normal. There were no nodes in the neck, and the roentgenogram of the chest showed no masses that might be compressing the trachea. The aortic arch seemed to be present on the right side. Bronchoscopy showed a marked narrowing of the trachea just proximal to the bifurcation. Purulent secretions were bubbling

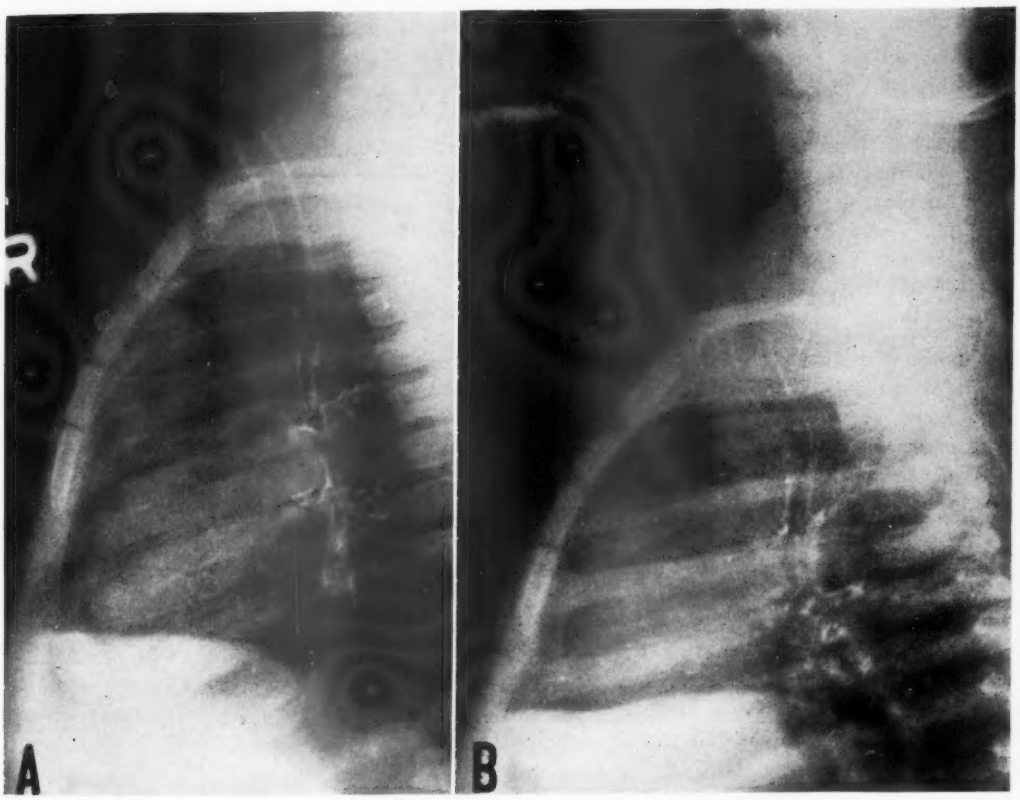

Fig. 4.—Tracheograms of second patient (*A*) before operation and (*B*) two weeks postoperatively.

up through the narrow lumen. These were aspirated and the bronchoscope could be passed readily through the narrowed area. There were vigorous pulsations of the trachea at the point of narrowing. Purulent secretions were further aspirated from both main stem bronchi, especially the right. An attempt was made to clear up the infection before surgery was undertaken. However, this was not entirely possible, as the atelectasis persisted and the purulent tracheobronchitis still was present after one week of intensive medical treatment. The only hope of improving the patient seemed to be in the relief of the tracheal constriction. Operation was, therefore, carried out.

A left posterolateral approach was made. After the thorax had been entered and the lung retracted anteriorly, the anterior limb of a double arch which was markedly constricting the trachea was visible through the mediastinal pleura. This is shown diagrammatically in Fig. 1. The anterior structure was the smaller of the two and did not

give rise to any branches. It was ligated as near to the main arch as possible, and divided. As it was divided the ends were seen to spring apart about two centimeters. As the anterior arch was being dissected the condition of the patient became extremely poor. The anesthetist could not maintain the airway, the patient became very anoxic, and the heart slowed down, almost ceasing to beat. It was manually massaged while the anesthetist changed the intratracheal tube. He had used a soft rubber tube which was collapsed by the constricting lesion. The constriction was apparently made worse by some shift of the mediastinum due to the thoracotomy. After a stiff noncollapsible tube had been passed down through the constricted area the airway was easily maintained, the heart immediately returned to normal action, and no further difficulties were encountered. The remaining arch and the ends of the divided arch were carefully dissected away from the trachea and eosphagus so as to leave these structures entirely free from the vascular ring. The lung was re-expanded and the chest wall closed.

For a few days postoperatively there were some tracheal secretions which had to be aspirated. The patient, however, no longer had the tracheal rattle, and the respirations were essentially normal. The cough disappeared within a week of the operation. The temperature returned to normal three days postoperatively and remained so. The patient was discharged two weeks after operation and remained well. Fig. 2 shows tracheograms made (a) before the operation and (b) two weeks afterward. This child is seen in Fig. 3 one year after operation. Up to that time there was only one slight respiratory infection which cleared up promptly.

CASE 2.—This girl was fourteen months of age when first seen. She had been in almost constant trouble throughout her life because of cough, a wheezing respiration which was noticed daily by the mother, and frequent respiratory infections. During the course of these infections she was always critically ill and several times it was thought she would not survive the acute attacks. There was extreme dyspnea present with the slightest respiratory infection. A moderate degree of cyanosis existed during the height of the infection.

A preliminary bronchoscopy showed that the trachea was markedly narrowed just above the carina. There was a moderate amount of mucopurulent secretion present, at the site of the narrowing and below, in both bronchial trees. Pulsations of the trachea were unusually great. The child was treated conservatively for a few days both by the intramuscular and inhalation type of penicillin. Tracheograms made before and after the operation are shown in Fig. 4. A chest roentgenogram showed the lung to be clear. The aortic arch was present on the left side. The heart seemed normal by clinical examination, by electrocardiogram, and by x-ray examination. There were no masses in the thorax that might be constricting the trachea.

Operation was performed, using a left posterolateral approach, and entering the thorax through the fourth intercostal space. During anesthesia a noncollapsible intratracheal tube was used. Upon inspection of the aorta, it was seen that a normal left arch did exist, as well as a normal descending aorta. The branches of the aorta were normally placed and of normal size and the double structure was not apparent at first inspection. It was necessary to mobilize the distal portion of the arch and the upper descending aorta. This was accomplished by ligating two pairs of intercostal arteries and mobilizing the left subclavian artery and aorta downward for a distance of about two inches. The posterior aspect of the descending aorta had to be brought into view before the posterior limb of the double arch could be visualized. This is shown diagrammatically in Fig. 5. A photograph taken at the time of operation (Fig. 6) shows a curved hemostat around the posterior limb which passes posteriorly to the trachea and esophagus. The posterior arch was thoroughly dissected away from the esophagus and trachea, following which it was divided and the ends sutured with fine silk sutures. The normal anterior arch which was adherent to the trachea was also completely dissected away from it. Very firm perivascular tissue adhered these structures to each other. The aorta was

allowed to fall back in its normal position and the pleura was closed over it. The child developed a laryngeal edema twelve hours after the operation and required a tracheotomy. Aside from this complication, she made a speedy and uneventful recovery. Fig. 7 shows a photograph of this child two months after operation. The mother stated that there had been only one slight respiratory infection during this time and that this quickly cleared. There were no wheezing respirations to be heard and no cough was present.

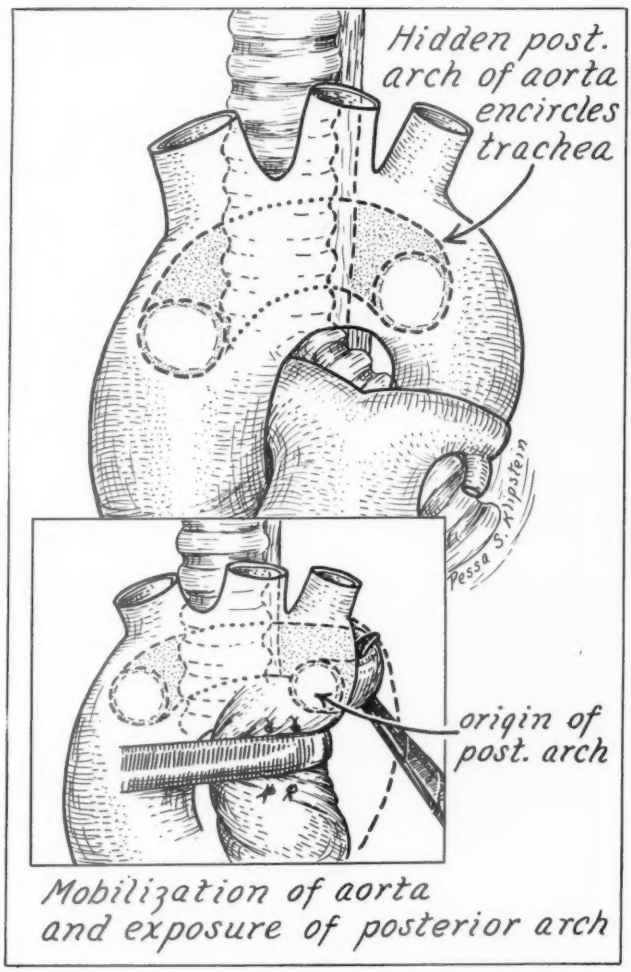

Fig. 5.—Diagram of double arch in Case 2.

DISCUSSION

In the first patient a fatality nearly occurred because of the collapse of the trachea during the operation. Had it not been for the alertness of the anesthetist* in changing the intratracheal tube from a soft to a hard type, death certainly would have occurred. The collapse of the trachea due to the vascular structures may be further aggravated by mediastinal shift. Gross apparently encountered this during his first operation for this anomaly. It would seem wise, therefore, to intubate these patients with stiff intratracheal tubes so that

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Fig. 6.—Photograph at time of operation in Case 2, showing a curved hemostat around the posterior limb. This arises just below the level of the left subclavian artery, the origin of which is shown. Trachea and esophagus are seen constricted between the two arches. A ligated intercostal artery is seen on the descending aorta.

Fig. 7.—Photograph of patient in Case 2, two months postoperatively.

the trachea cannot collapse at the point of constriction, although this does carry some risk of laryngeal edema and subsequent tracheotomy, especially in the young child.

Upon exploring the arch, the surgeon should completely mobilize it if this is necessary in order to find the double structure, because the posterior limb may arise from the buried surface of the arch and may not be identifiable by palpation or inspection. Potts[5] pointed out how he could have found the posterior limb in his first patient had he carried out this maneuver. Unsuccessful exploration for a constricting vascular ring is likely to result in the patient's death.

Although there may be some separation of the divided ends of the arch, the mere division of the structure may not be sufficient to completely remove the constriction from the trachea. This may account for the slow return of the trachea to normal in some of the reported cases. In both the cases reported here the lumen of the trachea returned to normal within two weeks and the relief of the symptoms was prompt. Both ends of the divided arch, as well as the remaining arch, should be as completely dissected away from the trachea as possible because the adherence of the vascular structure to the trachea may prevent its complete re-expansion.

SUMMARY

1. Two successful operations for double aortic arch are reported.

2. Tracheograms before, and two weeks after, the operations showed the trachea to have returned to essentially normal caliber in both patients.

3. The relief of symptoms was prompt.

4. Emphasis is placed upon three points:

   (a) The use of a non-collapsible intratracheal tube during operation.

   (b) The mobilization of the aorta, if necessary, in order to find the double structure.

   (c) The complete dissection of the vascular ring from the trachea and esophagus.

REFERENCES

1. Sprague, H. B., Ernlund, C. H., and Albright, F.: Clinical Aspects of Persistent Right Aortic Route, New England J. Med. **209**: 679, 1933.
2. Gross, R. E.: Surgical Relief for Tracheal Obstruction from a Vascular Ring, New England J. Med. 233: 586, 1945.
3. Sweet, R. H., Findlay, Charles W., Jr., and Reyersbach, Gertrude C.: The Diagnosis and Treatment of Tracheal and Esophageal Obstruction Due to Congenital Vascular Ring. J. Pediat. 30: 1, 1947.
4. Gross, R. E., and Ware, Paul F.: The Surgical Significance of Aortic Arch Anomalies, Surg., Gynec. & Obst. 83: 435, 1946.
5. Potts, W. J., Gibson, Stanley, and Rothwell, Robert: Double Aortic Arch. Report of Two Cases, Arch. Surg. 57: 227, 1948.
6. Bahnson, Henry T., and Blalock, Alfred: Aortic Vascular Rings Encountered in the Surgical Treatment of Congenital Pulmonic Stenosis, Ann. Surg. **131**: 356, 1950.
7. Griswold, Herbert E., and Young, Maurice D.: Double Aortic Arch, Pediatrics 4: 751, 1949.

AIR EMBOLISM IN OPERATIONS DONE IN THE SITTING POSITION

A Report of Five Fatal Cases and One of Rescue by a Simple Maneuver

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MEDICAL literature contains a considerable amount of information concerning air embolism, but little pertaining to its occurrence during the course of operations done in the sitting position. Among neurosurgeons the topic has been discussed uneasily and some men have abandoned the position after a few unhappy experiences. Our anesthesiologists also have been actively concerned with the problem.

CASE REPORTS

Case 1 (No. 95-611).—On Feb. 26, 1936, a cordotomy was being done on a 43-year-old woman to relieve her of pain in the back and legs caused by extension of a carcinoma of the cervix. The patient had been anesthetized by the rectal instillation of tribromoethanol in amylene hydrate and was sitting in the chair regularly employed for surgery of the suboccipital and upper spinal areas. The laminas of the seventh cervical and first dorsal vertebrae had been resected and the dura had been exposed when suddenly the patient made three or four rapid, grasping respirations and ceased breathing. The anesthetist administered a mixture of oxygen and carbondioxide under pressure with a face mask and respirations began again, but irregularly. Believing the respiratory abnormality to be temporary, the anesthetist allowed the operation to proceed. The dura was incised vertically and breathing ceased. Artificial respiration was begun again and several stimulants were administered subcutaneously. The pulse was imperceptible. The wound was covered, the drapes removed, and the back of the chair was dropped to allow the patient to recline. Artificial respiration was continued, and adrenalin was injected into the heart, but to no avail; the patient was dead. Observers were struck by a peculiar marbled appearance of the patient's skin.

At autopsy the jugular and larger thoracic veins were found to contain air bubbles. The right side of the heart was distended, and when it was opened the auricle and ventricle were found to be filled with frothy blood and a few blood clots. There was foamy blood in the pulmonary artery, the pulmonary vein, and a little in the left auricle. The left ventricle was empty; the foramen ovale was closed. The carcinoma of the cervix was found to have metastasized to the liver and to have extended into the bladder, the sciatic nerve, and the right iliac vein. Diagnosis was made of air embolism; its origin baffled us.

Case 2 (No. 135-089).—Four years later, a colleague performed a high cervical cordotomy in the sitting position upon a 44-year-old woman to relieve the pain caused by the extension of a carcinoma of the breast into the axilla. All went well until the dura was being closed, when again the peculiar coughing, gasping respiration was heard and the anesthetist reported that the systolic blood pressure had fallen from 140 to 60 mm. of mercury. Intravenous fluid administration was speeded up; the blood pressure rose to 90 mm., then became unobtainable. The wound was closed rapidly and the patient was lowered to the supine position. Again the marbled skin was noticed. All attempts at resuscitation were futile. Again the pathologist found the right side of the heart distended. When the right auricle was punctured in the pericardial sac, air bubbles streamed to the surface. When the heart was opened, the right auricle and ventricle were found to be filled

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with foam that extended into the main stem of the pulmonary artery. There was no air in the jugular vein or the superior vena cava. In this case the foramen ovale was patent (1 by 0.5 cm.) and there was a small amount of foam in the left auricle. The brain was found to be essentially normal.

Naturally, we became greatly concerned over the mechanism of this catastrophe. Only one other case (No. 103-752) of the air embolism had occurred in the Buffalo General Hospital; that had followed uterine dilatation and curettage and the insufflation of air to test the patency of the uterine tubes. It was decided that in our cases the sitting position favored the development of the emoblism through veins opened above the level of the heart. The advantages of the sitting position for this type of surgery were so great, however, that other methods were sought to prevent this complication without abandoning the position. The best solution appeared to lie in flooding the surgical field frequently with normal saline solution during the laminectomy, cauterizing the visible epidural veins, and waxing the raw bony edges.

No similar complication occurred in the following seven years. Then, at the completion of a temporal, sensory, trigeminal rhizotomy (No. 187-707) in an elderly patient, the blood pressure fell and did not respond to stimulants. By the time the patient was lowered to the supine position, the heart had stopped. The clinical picture of air embolism was not recognized here, but was found at autopsy. The site of entry apparently was a pinhead-sized opening in a venous tributary to the cavernous sinus. Ten months later the castastrophe occurred again at the termination of a cervical cordotomy (No. 193-583).

Three months later a patient (No. 195-918) died shortly after he had been returned to his room following a vestibular rhizotomy. The respirations had become difficult at the end of the operation and the blood pressure had fallen to 60 mm. of mercury, although this had increased to 100 mm. before he was lowered to the supine position. Autopsy again showed the right side of the heart filled with foam.

One of us (R. N. T.) found that Durant, Long, and Oppenheimer[1] had reported that dogs placed in the left lateral position survived the intravenous injection of quantities of air grossly in excess of volumes lethal to animals placed in the dorsal or right lateral positions. Also, it was reported, animals allowed to develop evidence of marked ventricular failure while lying on the back frequently recovered when turned onto the left side.

CASE REPORT

CASE 3 (No. 222-402).—On Feb. 8, 1951, it became necessary to remove a cervical intervertebral disc protrusion in the case of a young mother who was the sole support of three small children. Despite its hazards, the sitting position was chosen for the operation and all known precautions were taken against the development of air embolism. Blood pressure was maintained carefully and the surgical field was flooded with normal saline solution frequently during the exposure of the affected nerve root. Nevertheless, as the almost freed nerve root was being displaced, the patient suddenly coughed, gasped, and ceased breathing. The surgical field became bloodless; the pulse and blood pressure were

imperceptible; on auscultation the heartbeat could not be heard. The wound was covered with a folded towel held by the surgeon, the drapes were removed, and the chair was flattened out. The anesthetist reported the heart beating wih a rapid, gurgling, "mill-wheel" murmur. While some assistants released the ties restraining the patient, several others hurriedly listened to the heart murmur, passing the stethoscope from hand to hand. As one of them was fitting the ear pieces, the patient was turned on the left side; he reported normal heart tones. Blood pressure rose at once to 110 mm. of mercury, the pulse became full and regular; respirations regained normal rate and volume. The operation was completed with the patient prone. No postoperative complications developed and the patient returned to her home on the fourteenth postoperative day.

DISCUSSION

Martland,[4] commenting upon the surgical importance of air embolism, has distinguished the clinical features of air introduced into the venous system from those of air introduced into the arterial system. Arterial air embolism produces its effects by blocking either the coronary or the cerebral arteries.

When a relatively large volume of air reaches the right auricle via the venous system, a cardiac tampon of foamed blood is produced. Because of its compressibility, this is difficult to express, so a considerable quantity of air remains in the ventricle after each systole. The right auricle and ventricle distend and pulmonary circulation is blocked. Death is due to interference with proper ventricular systole. In open-chest experiments, Durant and co-workers[1] found that the right ventricle labors against the obstruction of an air trap in its outflow tract when position makes this the uppermost part of the right heart, as when the animal is on its back or right side. When the animal is turned on the left side, the outflow tract assumes a position inferior to the body of the right ventricle. The air trap disappears, presumably churned to a froth and mixed with blood in the right ventricle. The blood is propelled by ventricular contractions into the pulmonary artery, thence into the lungs where it is excreted.

Systemic (arterial) air embolism may complicate venous air embolism by passage through a patent foramen ovale. This passage may be closed physiologically by the normally higher pressure in the left side of the heart. In the presence of venous air embolism, right heart pressure may approach ten times the normal pressure due to air blockade of the pulmonary circuit. Sudden death may follow coronary occlusion or various neurologic complications may result from cerebral air embolism. Air has been observed to pass the pulmonary capillary bed by unexplained avenues where no patent foramen could be demonstrated at autopsy. Martland[4] listed the marbled appearance of the skin as a sign of arterial air embolism; this phenomenon was noticed in two of our five fatal cases. A patent foramen ovale was found in one of these patients, but not in the other. Air bubbles have been observed by ourselves and by other neurosurgeons in cerebellar arteries of patients operated upon in the sitting position.

Study of our five fatal cases of air embolism suggests that the condition may manifest itself abruptly or may remain unrecognized until autopsy. In the latter instances only respiratory irregularities, a fall in blood pressure difficult to restore, and a feeble pulse may suggest the diagnosis. Our experience does not indicate whether the swishing, "mill-wheel" heart murmur is heard in these

cases; it was identified only in our final case. It seems quite possible that the death of some patients shortly after being returned to their beds in "shock" may be the result of air embolism.

The patients with abrupt manifestations of the accident display them with recognizable signs. The first warning is a deep inspiration, followed by a coughing exhalation, then a few ineffective attempts at breathing, succeeded by apnea. The previously satisfactory blood pressure reading falls to a low or unrecordable level. The pulse becomes imperceptible. The cardiac sound is inaudible with the patient sitting, but when the patient is shifted to the supine position, the heart sound returns with a to-and-fro, swishing, "mill-wheel" murmur.

In personal communications we have learned of two other victims of air embolism being rescued by this maneuver. Durant told us of "a young woman blood donor who developed air embolism because of a flask which had lost its vacuum. She recovered when turned into the left lateral position, but there is a possibility that she might have recovered under any circumstance, since the amount of air was apparently not very great." Dr. W. E. Chamberlain reported a patient who developed air embolism during the performance of an adrenal gland aerogram. This patient also was rescued because of knowledge of the position recommended by Durant and his co-workers.

Three other references have been found in the literature concerning patients rescued from the effects of air embolism. Stallworth and co-workers[5] while performing a laparotomy, noticed the signs of air embolism. A 20 gauge lumbar puncture needle was introduced into the right ventricle, 15 c.c. of air were aspirated, and circulation recovered. Lembcke[3] reported a recovery under similar circumstances when the air embolism had occurred during hysterectomy. Fulcher[2] reported saving a patient by forcing 3 liters of saline solution into the vein under great pressure. The embolism had occurred during venoclysis in which air pressure was employed to facilitate the procedure.

SUMMARY

Five cases are reported in which fatal air embolism developed during the course of neurosurgical operations performed in the sitting position.

Abrupt and delayed forms of the castastrophe have been found.

In one case, a simple postural method of resuscitation was found. The patient was immediately shifted into the left lateral position.

REFERENCES

1. Durant, T. M., Long, J., and Oppenheimer, M. J.: Pulmonary (Venous) Air Embolism, Am. Heart J. **33**: 269-281, 1947.
2. Fulcher, O. H.: Successful Treatment of Air Embolism. Report of Case, M. Ann. District of Columbia **5**: 365, 1936.
3. Lembcke, W.: Ueber erfolgreiche Behandlung einer schweren Luftembolie durch Herzkammerpunktion, Chirurg. **17-18**: 31-35, 1946. (Abst. J. A. M. A. **136**: 140, 1948.)
4. Martland, H. S.: Air Embolism, With Special Reference to Its Surgical Importance, Am. J. Surg. **68**: 281-286, 1945.
5. Stallworth, J. M., Martin, J. B., and Postlethwait, R. W.: Aspiration of the Heart in Air Embolism, J. A. M. A. **114**: 1250-1251, 1950.

SIMULTANEOUS BILATERAL RADICAL NECK DISSECTION

Total Ablation of Both Internal and External Jugular Venous Systems at One Sitting

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MUCH difference of opinion still exists among those responsible for treating head and neck cancer as to the various methods of treating the primary tumors located in this area. However, no such difference of opinion exists concerning the treatment of cervical metastases arising from these primary tumors. It has now been generally accepted by most radiologists and surgeons alike that the method of choice in the treatment of cervical metastases is a radical neck dissection. By definition, the term "radical neck dissection" has now come to mean complete removal of all mobile structures in the neck with the exception of the carotid artery, vagus nerve, phrenic nerve, hypoglossal and lingual nerves; and hence the routine sacrifice of the internal jugular vein with all its tributaries, the sternocleidomastoid muscle, and the spinal accessory nerve together with all lymphoid and adipose tissue is widely practiced.

A glance at Fig. 1 will show the close relationship between the deep cervical lymphatics and the internal jugular vein. It is apparent from this close anatomic association that adequate removal of the deep cervical lymphatics can best be accomplished by removing the internal jugular vein. The writings of the earlier workers in neck surgery reflect hesitancy and fear of the consequences of interrupting the continuity of the internal jugular vein. Presumably, this was with the idea that grave disturbances in intracranial pressure would result from such a procedure. However, this practice has now been accepted, and its safety has been proved repeatedly by the survival of literally hundreds of patients. Accordingly, interruption of one internal jugular vein no longer troubles surgeons dealing with head and neck cancer.

Only recently have the consequences of interruption of both internal jugular systems been more thoroughly explored. A survey of the literature reveals that a fair number of cases have now been reported in which bilateral neck dissections have been carried out. In the majority of instances, however, the second operation has been carried out at intervals varying from seven days to several months or years following the initial procedure. There are only a few scattered reports describing simultaneous interruption of these two systems.[1-5] The associated mortality rate was so prohibitive in these cases as to discourage further practice of this procedure.

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EARLY REPORTS OF SIMULTANEOUS BILATERAL INTERRUPTION OF BOTH INTERNAL JUGULAR VEINS

In surveying the earlier writings on this particular subject it becomes evident immediately that the cases under consideration may be broadly divided into two groups. The first group comprises those cases in which the internal jugular veins were ligated as an isolated surgical procedure. This usually was practiced for cases of sinus thrombosis resulting from suppurative mastoiditis with the objective of preventing further extension of the septic thrombosis. In such cases as these the collateral circulatory bed may be considered to be practically undisturbed by such an operation. In the second group of cases, surgeons have employed more extensive operations, usually aimed at the control or eradication of cervical metastases or bilateral tuberculous adenitis.

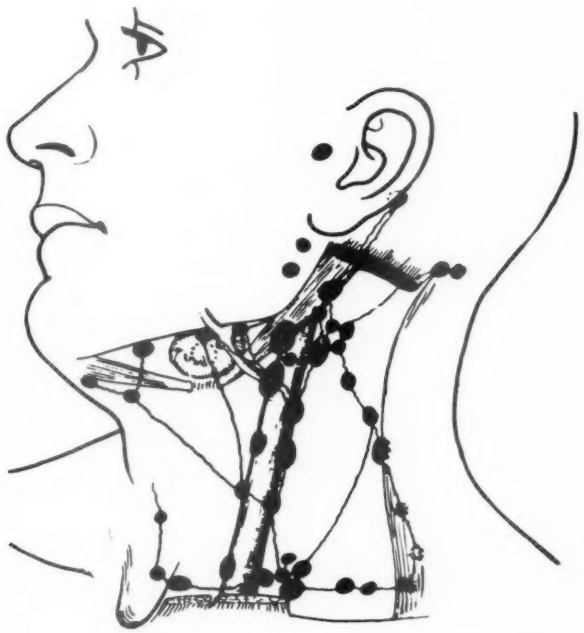

Fig. 1.—Diagrammatic representation of cervical lymphatics (after Martin). The lymph nodes in the neck occur with regularity at definite fixed locations. The close association of the deep nodes surrounding the internal jugular vein, thereby necessitating sacrifice of this structure in the course of the neck dissection for cancer, is clear.

It is readily seen that the amount of tissue sacrificed in the course of these latter extensive operations is considerably greater, and as a consequence there is a correspondingly increased disturbance not only of the main venous channel (internal jugular veins) but also of a great many of the superficial collateral channels. Because of this basic fact, a detailed discussion of the cases in the first group will be omitted here since it is felt that they can hardly be said to constitute a valid comparison with our current problem.

I am indebted to the excellent review by Evans[5] of the earlier literature on this topic. I have been unable to find any earlier case of bilateral internal jugular vein interruption associated with a major surgical procedure in the

neck than that of Ewald.[1] This surgeon, in 1900, resected both jugular veins during an extensive operation for cervical metastases. The report states that the patient died following this procedure without ever having regained consciousness. Ewald assumed that death was on the basis of a "vasomotor disturbance."

Baldwin,[2] in 1902, reported a case of synchronous ligation of both internal jugular veins in the course of removing tuberculous masses from the neck. This patient survived. It is possible that at least one explanation for the survival may be that the operative attack was considerably more limited than that usually carried out in the modern radical neck dissection.

Max Dangel,[3] in 1905, again performed this operation in the course of an attempted removal of bilateral cervical metastases. This patient also survived.

In 1909, Duval[4] reported three cases in which the internal jugular veins had been ligated but in only one of these cases was the ligation carried out simultaneously. This was the first case of simultaneous bilateral radical neck dissection and his graphic description may be quoted here: "Immediately following the ligation of the second jugular vein the patient's face became not only violet but black. This discoloration gradually extended down to the neck and soon the respirations ceased. Suddenly the patient had a profuse hemorrhage from the mouth and throat of dark blackish blood. After this spontaneous venesection the patient began to breathe again and his face became violet, then pink. It was then possible to complete the operation. Except for a slight facial violet tint lasting for two hours together with considerable parotid swelling for a day, the postoperative course was uneventful. Thirteen days later the lower maxilla, chin tissues and a part of the floor of the mouth were resected and the patient made a good recovery."

Somewhat chastened by this awesome experience in his first case, Duval decided to stage ligation of the veins, and in his second case an interval of sixteen days separated the two procedures. Despite this fact the patient died. Immediately prior to his death there was marked suffusion of the soft tissues and conjunctiva at which time the patient remarked that he did not feel well. He died within a few minutes after uttering this observation. The operations in the two preceding cases had been carried out for removal of cancer and this was the situation in the third case as well. An interval of one month elapsed between the two neck dissections in this case. Death occurred on the third postoperative day having been preceded by cyanosis and swelling of the soft tissues with apparent increasing difficulty in respirations.

The *Quarterly Cumulative Index Medicus* does not contain any reference which by title would indicate that this procedure has been carried out, or if so, that an account of it has been published over the period intervening between Duval's cases and the present time. (Evans' cases consisted of simple ligature of both internal jugulars to forestall spread of a septic thrombosis following suppurative mastoiditis.) Dr. Oliver Moore of the Head and Neck Service at Memorial Hospital, New York,* described five cases of simultaneous bilateral neck dissection done without a fatality. Sugarbaker,[6] at an earlier meeting

*In a verbal report to the James Ewing Society in 1951.

(1950) of the same society, described methods of study of intracranial pressure changes following vein ligations which suggested certain counter measures which will be outlined under Operation and may prevent fatalities from this procedure.

CASE REPORTS

History.—The patient was a 64-year-old white woman who entered the Bonfils Tumor Clinic on Dec. 18, 1950. At that time she gave a history of having had a squamous carcinoma of the lower lip treated by irradiation approximately two and one-half years previously. This primary lesion had been located in the midline of the vermilion border. There was an excellent response to the radiation therapy as evidenced by no recurrence following the conclusion of the treatment. No effort had been made to follow the patient for possible recurrences or metastatic spread to the cervical nodes, however.

About six months prior to admission she first became aware of a swelling beneath the horizontal ramus of the right mandible. At this time she was having several teeth extracted and it was assumed by the patient and her dentist that this mass represented an inflammatory lymphadenitis. Accordingly, she was treated with penicillin but the mass continued to progress in size and became fluctuant. Because of this finding the assumption was then made that the swelling represented "a salivary cyst." The fact that on repeated aspirations fluid was obtained from the mass with resultant decrease in size was interpreted as corroboration of this diagnosis. However, in a matter of a day or two following each aspiration the mass quickly filled up again and regained its previous size. About three weeks prior to admission to our clinic a similar mass appeared in the left submaxillary triangle. The dentist became alarmed at this and requested a medical consultation. The patient was referred to a physician* who again aspirated the mass but saved the contents and sent them to the laboratory where numerous cells of squamous carcinoma were seen in the sediment. The diagnosis of metastatic cervical cancer, secondary from a previously treated lip cancer, was then made and the patient referred to the Bonfils Tumor Clinic for further care.

Examination.—The site of the primary tumor in the midline of the lower lip was indicated only by slight telangiectasia. There was no evidence of recurrence at this site. Centered in the region of the right submaxillary triangle there was a large cystic mass which appeared fixed to the mandible and measured 8 by 7 cm. The mass in the left submaxillary triangle measured 5 by 5 cm. but did not appear fixed to the mandible. X-ray examination of the right mandible failed to reveal any evidence of gross bone destruction (see Fig. 2).

Impression.—Carcinoma of the lower lip, postirradiation, with bilateral cervical metastases.

Recommendation.—Although the x-ray examination failed to reveal any gross evidence of bone destruction in the right horizontal mandible it was evident from clinical examination that this large mass was so closely associated with this structure that a portion of it would have to be sacrificed if a wide margin was to be attained. Our conclusions may be summed up by the following representative note taken from the chart: "My preference would be to do a combined neck and jaw resection on the right side first and give the patient a chance to recover from this procedure before taking care of the left side. However, I am afraid that if we wait another three weeks or more the mass on the left side will have grown to such proportions as to necessitate sacrifice of a portion of the left jaw as well. Accordingly, the patient is to be admitted for a combined neck and jaw resection on the right side followed at the same sitting with a left radical neck dissection."

Operation.—On Dec. 20, 1950, a right radical neck dissection together with a partial jaw resection was carried out, followed by a left radical neck dissection. Prior to operation a continuous spinal needle was placed into the fourth vertebral space as suggested by Sugarbaker and Wiley and manometric readings were recorded both preoperatively and during the operation. The changes in the cerebrospinal fluid dynamics are indicated in the chart (Fig. 3). It will be seen from this graph that no marked rise in the cerebrospinal fluid

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pressure was attained until the interruption of the second jugular vein in the course of the neck dissection on the left side. At this time there was a rise to approximately 420 mm. of water. This represented the maximum rise at any time during or after the operative procedure.

It is quite probable that the pressure would have risen to higher levels had it not been for the fact that each time an abnormal reading in the cerebrospinal fluid pressure was attained, this was countered by drawing off fluid through the continuous spinal needle. Enough fluid was drawn off each time to restore the cerebrospinal fluid pressure halfway back to the normal levels. The amount of fluid drawn off varied from 10 to 25 c.c. Within forty-eight hours after the operation repeated spinal taps were showing normal values, and accordingly no further efforts were made to drain off any more spinal fluid. The edema of

Fig. 2 (Case No. 30092).—Anteroposterior and lateral views taken preoperatively. Note the large masses centered in the region of the submaxillary triangles. Aspiration biopsy on both of these masses was returned as positive for metastatic squamous carcinoma.

the soft tissues of the pharynx and larynx was anticipated and to counteract this complication a tracheostomy was done as a part of the original operative procedure to insure that the patient had an adequate airway. The blood pressure did not vary significantly during the procedure (Fig. 4).

Postoperative Course.—Largely due to the administration of 1,500 c.c. of whole blood, the patient returned to the ward without ever having approached a shock level at any time during the operative procedure. She regained consciousness within three hours after her return to the ward and was able to get up and use a bedpan the same evening. The anticipated edema of the eyelids, pharynx, larynx, and all the soft tissues in the head and neck developed but there was never any compromise of the airway due to the previously constructed trache-

ostomy (Fig. 5). A diet containing adequate nutritional requirements was administered through an indwelling nasogastric catheter. Due to the tremendous edema of the pharyngeal muscles and the intrinsic musculature of the tongue the patient was unable to swallow anything except saliva for approximately seven days. There was also extreme limitation of motion of all muscles in this area (strap muscles, constrictors, intrinsic tongue muscles, etc.) presumably due to this marked edema.

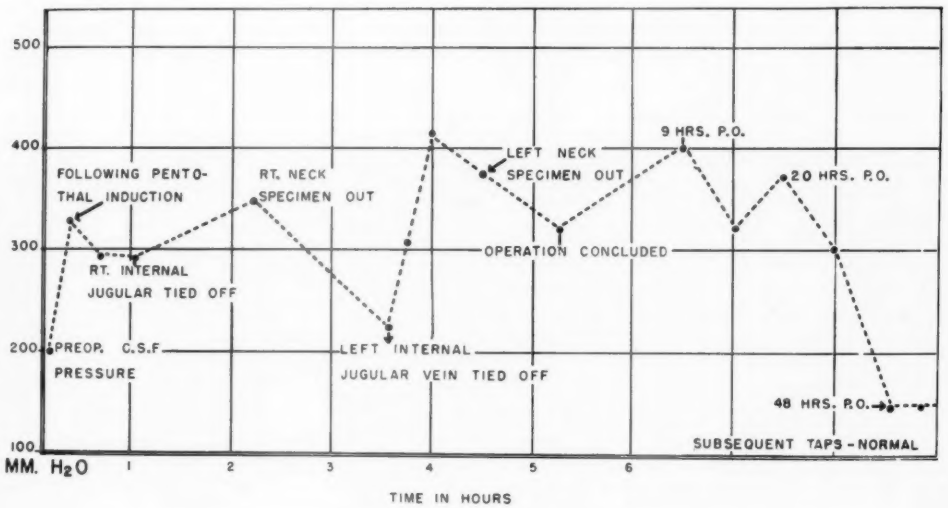

Fig. 3 (Case No. 30092).—Concomitant changes in cerebrospinal fluid pressure.

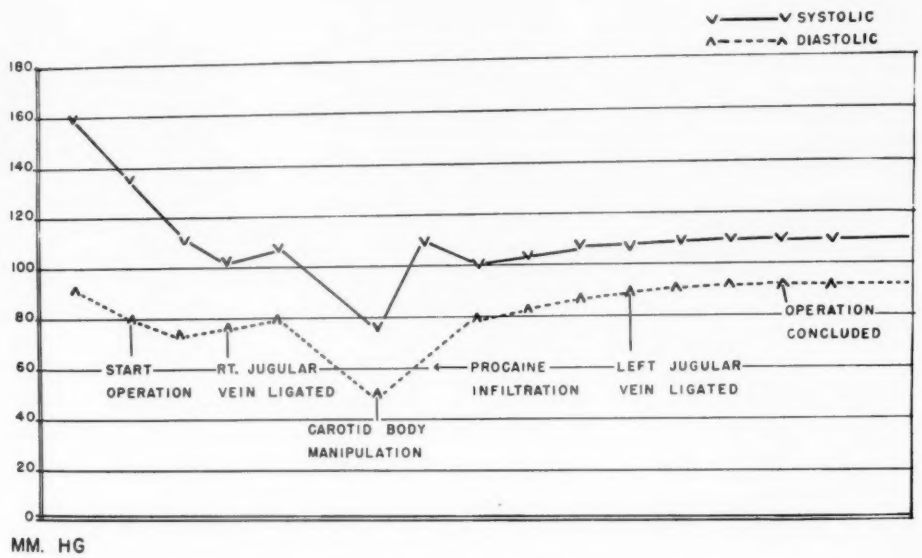

Fig. 4 (Case No. 30092).—Concomitant changes in blood pressure.

There was steady but gradual improvement in this status during the ensuing few weeks so that it was possible to remove the tracheostomy tube at the end of seventeen days although it was still necessary to continue nasogastric feedings for another two weeks. The patient was discharged from the hospital on Jan. 31, 1951 (forty-two days postoperatively).

Pathology Report.—The pathology examination confirmed the presence of bilateral metastatic squamous carcinoma. However, despite the massive size of the large masses in

the submaxillary triangles, examination of the remainder of the nodes in the neck failed to reveal similar spread of disease. The tumor was seen to be invading the periosteum of the resected portion of the right mandible but the bone structure itself was not touched by the disease process.

Follow-up Report.—The patient has returned to her daily activities and returns now at monthly intervals for checkups. There has been almost complete subsidence of the facial edema and the patient is eating and talking quite normally. Headaches have been a nuisance to the patient if she subjects herself to heavy exercise. Under ordinary activities there is no such complaint present. The headaches are becoming less intense and of less frequent occurrence in recent weeks as the clinical evidences of restoration of collateral circulation through other channels has become increasingly apparent (Fig. 6).

Fig. 5 (Case No. 30092).—Views of patient *A*, seven days, and *B*, fourteen days post-operative. Note the tremendous edema of the soft tissues. Complete obstruction of the airway and hypopharynx was countered by tracheostomy and a nasal feeding tube.

DISCUSSION

There will not be many instances in which such a procedure as has been outlined in this paper will be indicated. A patient suffering from head and neck cancer is more likely to present himself with a unilateral primary cancer with or without corresponding homolateral cervical metastases. The definitive efforts at therapy at this stage consist of attempts to eradicate the primary tumor with later or concomitant surgical attack on the cervical metastases. If such a patient develops metastases on the opposite side of the neck, it is more common to see this occur after an interval of time measured usually in terms of months. This interval between the time when the metastases are treated on the first side and when they subsequently develop on the opposite side usually serves to supply sufficient time so that adjustments via collateral pathways can be established.

Under most circumstances when the patient presents himself initially with bilateral cervical metastases, the chances are greatly in favor of the tumor being so extensive that achievement of permanent control is highly unlikely. Other possibilities that may explain the presence of bilateral cervical metastases would be the presence of a primary lesion in the nasopharynx or some similar situation where attempts at control by radiation therapy must be relied upon. In such circumstances, it is doubtful whether such an aggressive procedure as that described here is wise.

Fig. 6 (Case No. 30092).—View of patient three and one-half months postoperative. Marked subsidence of soft tissue edema with more complete healing and wider development and usage of collateral return channels. Patient now eating and speaking normally.

Nevertheless, there will undoubtedly be selected cases from time to time in which radical surgery has much to recommend it. Many lip cancers, for example, occur in the midline and therefore metastasize to both sides of the neck. Of all forms of intraoral cancer, lip cancer carries the best prognosis and com-

pared to cancers of the tongue, tonsil, etc., it is a much less aggressive disease. Under such selected circumstances it is possible that cures may be attained by simultaneous bilateral neck dissections. It will be helpful to surgeons dealing with such problems to be familiar with the points discussed here.

The reader is referred to any standard textbook of anatomy or to the specific study of Gius and Grier[7] concerning the mechanics of venous circulation in the head and neck. It is apparent that although the internal jugular veins and the vertebral veins come to mind first as the main channels of blood return for the brain, nevertheless, there are literally tens of other pathways that can be called into service in the event of necessity. In general these pathways may be considered to fall into three groups: (1) vertebral pathways, (2) the pathways traversing the internal soft tissues of the oropharynx, pharynx, etc., and (3) the pathways traversing via the scalp and thence through superficial cutaneous, subcutaneous, and preserved muscle groups (scalenus, spinalis cervicus and capitus, trapezius, etc.). Again it is important to bear in mind the difference between simple ligation of the internal jugular vein, as practiced by many older nose and throat men for suppurative septic thrombi of the sigmoid sinuses, and ligation of the internal jugular veins associated with marked interruption of collateral channels that comes with the execution of bilateral radical neck dissection.

COMMENT

It seems apparent from this case report as well as from experience with other operative procedures in the head and neck that the danger of immediate mortality following these radical procedures comes first of all from respiratory obstruction resulting from postoperative edema. This threat can be surmounted by the routine adjunct of a tracheostomy which will serve until the edema has subsided and exchange by the normal pathways can be resumed.

In addition to this already established procedure we now endorse routine checks on the status of the cerebrospinal fluid pressures whenever an acute interruption of a large share of the venous bed is to be an inevitable part of the operative procedure. For practical purposes, the latter can be said to be almost entirely limited to those isolated instances when simultaneous bilateral neck dissections are planned, or when the interval between the two-stage procedures is of such short duration that doubt as to the efficacy of the collateral channels exists.

SUMMARY

Acute interruption of the venous return from the head and neck is well tolerated by the patient if limited to one side. If it is necessary to produce acute interruption of these channels on both sides of the neck, certain complications which may prove fatal should be anticipated. These consist primarily of increased intracranial pressure and edema of the soft tissues sufficient to produce respiratory obstruction.

Surgeons dealing with head and neck cancer will occasionally be confronted with a desperate situation where bilateral radical neck dissection at one sitting may afford the only possibility of cure. Provided the above complications of

increased intracranial pressure and respiratory obstruction are countered by repeated spinal taps and a routine tracheostomy, the patients will survive such operative attack. A case report is outlined illustrating these methods.

REFERENCES

1. Ewald, C.: Tod unter vasomotorischen Störungen nach Resection beider Venae jugulares internal, Wien, klin. Rundschau **14**: 673, 1900.
2. Baldwin, J. F.: Synchronous Ligation of Both Internal Jugular Veins, Ann. Surg. **36**: 394, 1902.
3. Dangel, Max: Ueber die Unterbindung den Vena jugularis interna—Ein Fall von doppel seitiger Unterbindung, Beitr. z. klin. Chir. **16**: 495, 1905.
4. Duval, M.: Ligature des Deux Juulares Internes, Bull. et mém., Soc. de chir. de Par. **35**: 224, 1909.
5. Evans, Maurice: Bilateral Jugular Ligation Following Bilateral Suppurative Mastoiditis, Ann. Otol., Rhin. & Laryng. **51**: 615, 1942.
6. Sugarbaker, E., and Wiley, H. M.: Intracranial Pressure Studies Incident to Resection of Internal Jugular Veins, Cancer, 242, 1951.
7. Gius, John Armes, and Grier, Dugald H.: Venous Adaptation Following Bilateral Radical Neck Dissection With Excision of the Jugular Veins, SURGERY **28**: 305, 1950.

THE EFFECT OF SURGERY ON THE PLASMA LEVELS OF THE INDIVIDUAL ESSENTIAL AMINO ACIDS

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A DISTURBANCE in protein metabolism indicated by an increased excretion of nitrogen following operation has been noted by numerous writers.[1, 2, 4, 5, 22] At the present time there is no completely satisfactory explanation of this excessive nitrogen loss which occurs following major surgical procedures or trauma. In 1946, Man and co-workers[21] noted that the plasma alpha amino acid nitrogen level fell abruptly after surgery and remained low until recovery was well advanced, even while nitrogen catabolism was greatly increased by the administration of high protein diets. They suggested that the lowered concentration of amino acid nitrogen in the plasma might indicate that the production of urea was so active in the liver that the tissues were deprived of the amino acids required for the production of protein.

In view of these findings of Man and co-workers, a study has been made of the effect of surgery on the plasma levels of each of the individual essential amino acids in an effort to determine if a definite derangement in the metabolism of one or more of the essential amino acids (as indicated by abnormal plasma level) occurs in the catabolic period following operation. Such evidence of impairment in the metabolism of specific essential amino acids during the postoperative period might aid in explaining the increased nitrogen loss which occurs following surgery.

REVIEW OF THE LITERATURE

There have been no previous studies of the effect of surgery on the plasma levels of the individual essential amino acids. There have been only a very few studies of the effect of surgery on the level of plasma amino nitrogen. In 1936 Lürje[19] reported an increase in plasma amino nitrogen following operations. In 1942, Farr and co-workers,[7] on the other hand, reported a fall in plasma amino acid nitrogen following nitrous oxide and ether anesthesia and surgery. In nine children the concentration of amino acid nitrogen in plasma decreased on the average 0.38 mg. per 100 ml. following the induction of anesthesia, with a further decline averaging 0.46 mg. per 100 ml. during a surgical procedure. In five of the nine patients plasma amino acid concentration was lower two hours after operation than at the conclusion of the operative procedure.

As previously mentioned, Man and co-workers,[21] in 1946, noted that plasma alpha amino acid nitrogen fell abruptly after surgery and remained low until recovery was well advanced, even while nitrogen catabolism was greatly

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increased by the administration of high protein diets. In 1947, Man and co-workers[22] also reported the effect of prefrontal lobotomy on seven schizophrenic patients. They again noted that the plasma alpha amino acid nitrogen dropped sharply one or two days after operation in the same manner that amino nitrogen fell in nonschizophrenic patients after major operations. (It is to be noted that in both of these studies by Man and her co-workers the first postoperative samples of blood for study of the amino nitrogen plasma levels were not drawn until the first postoperative day.)

METHODS

The effect of surgery on the plasma levels of the individual essential (free) amino acids was studied in sixteen patients. The patients, with two exceptions, were considered to be in good nutritional status prior to the operative procedures. The operations ranged in magnitude from cholecystectomy to gastric resection.

For the determination of the individual essential (free) amino acids of plasma 50 to 60 c.c. of blood were drawn preoperatively, immediately postoperatively, and on the morning of the first postoperative day. In eight of the patients, additional samples were drawn on the third and seventh postoperative mornings. The barrel of the syringe used in drawing the sample was coated with heparin and two drops of heparin were placed in the collecting tube to prevent coagulation of the blood. In all patients an additional sample of blood was drawn each time for the determination of serum proteins. Two cubic centimeters of the well-mixed heparinized blood were used for the determination of the hematocrit which was done in duplicate using Wintrobe tubes which were centrifuged at high speed for thirty minutes. The remainder of the heparinized blood sample was centrifuged at 3,000 r.p.m. for one-half hour to separate the plasma from the cells. The filtrate of the plasma was prepared according to the method of Hier.[10, 11, 12] Determinations of the levels of the ten individual essential (free) amino acids were then performed on the plasma filtrate using the microbiological assay methods of Hier and Bergeim.[10, 11, 12] Serum albumin and globulin were determined by Hoffman's modification of Howe's method.[14] All analyses were performed in duplicate. (In addition to the eight amino acids essential for maintenance in man, arginine and histidine were also determined because they are essential in certain lower animals.[26])

RESULTS AND DISCUSSION

The data obtained in this study are summarized in Table I and Figs. 1 and 2. The average plasma level of the total ten individual essential amino acids before surgery was 171.6 gammas per cubic centimeter of plasma. Immediately after surgery the mean plasma level of the total ten individual essential amino acids was only 137.7 gammas per cubic centimeter of plasma. By the morning of the first postoperative day the corresponding level was 161.0 gammas per cubic centimeter of plasma. The level on the third postoperative day was 164.9 gammas and on the seventh postoperative day 161.3

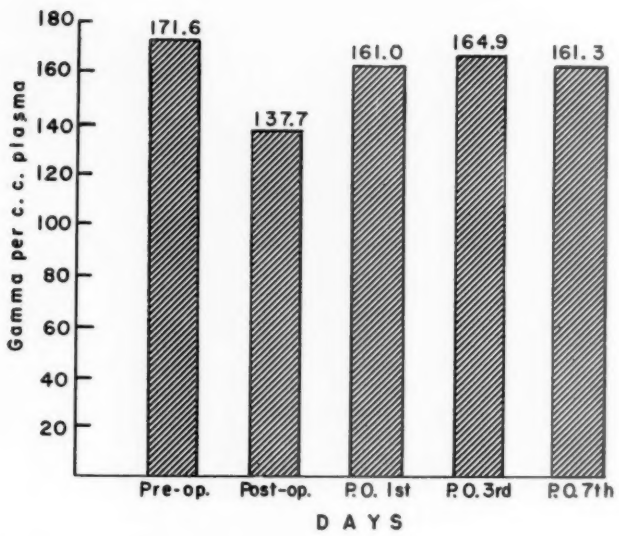

Fig. 1.—The effect of surgery on the average total of the ten essential (free) amino acids of human plasma.

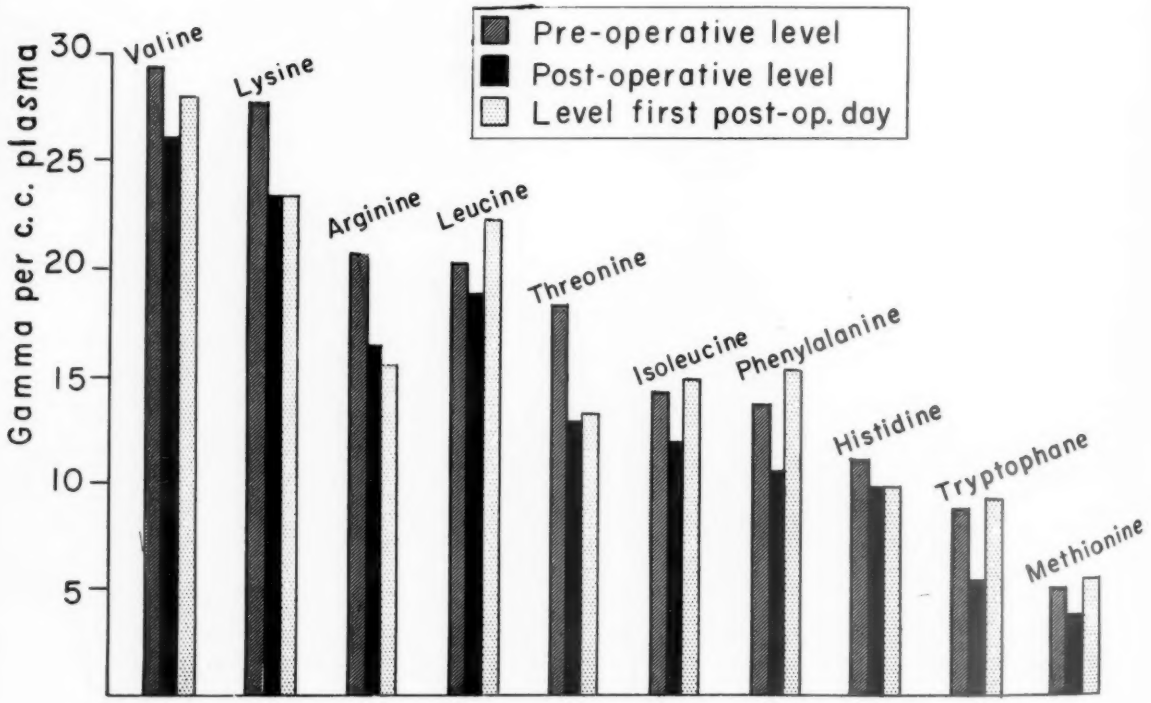

Fig. 2.—The effect of surgery on the individual essential (free) amino acids of plasma. (Average of sixteen patients.)

gammas per cubic centimeter of plasma. When these data were subjected to statistical analysis,[29] it was found that the differences between the preoperative, first postoperative day, third postoperative day and seventh postoperative day levels were not statistically significant. However, the plasma level immediately postoperative was significantly different from all of the other levels. The average decrease of the total ten essential amino acids immediately after surgery was 33.9 gammas per cubic centimeter of plasma, or a percentage reduction of 20 per cent.

TABLE I. THE EFFECT OF SURGERY ON THE PLASMA LEVELS OF THE INDIVIDUAL ESSENTIAL (FREE) AMINO ACIDS

	AVERAGE OF 16 PATIENTS (GAMMAS/C.C. PLASMA)			AVERAGE OF 8 PATIENTS (GAMMAS/C.C. PLASMA)	
	PREOPERATIVE	IMMEDIATELY POSTOPERATIVE	FIRST PO DAY	THIRD PO DAY	SEVENTH PO DAY
Leucine	20.2	18.7	23.0	22.8	20.7
Isoleucine	14.6	11.4	13.7	14.7	14.6
Tryptophane	9.1	5.5	9.6	9.1	8.7
Valine	29.2	25.8	31.1	31.4	26.6
Methionine	5.0	3.7	5.3	3.7	3.8
Threonine	18.5	13.0	13.6	14.3	16.3
Arginine	21.8	15.7	15.7	16.2	19.4
Phenylalanine	14.1	10.4	15.5	15.9	11.1
Histidine	11.5	10.1	10.1	10.2	9.7
Lysine	27.6	23.4	23.4	26.6	30.4
Total ten amino acids	171.6	137.7	161.0	164.9	161.3

Reference to Table I and Fig. 2 reveals that the mean plasma level of each of the individual essential amino acids likewise decreases following surgery. The magnitude of decrease of the plasma levels of the various individual essential amino acids following surgery varied from a mean decrease of 6.1 gammas per cubic centimeter of plasma for arginine to a mean decrease of 1.3 gammas per cubic centimeter of plasma for methionine. The percentage decrease of the plasma levels of the various individual essential amino acids following surgery varied from an average percentage reduction of 40 per cent for tryptophane to an average percentage reduction of 7 per cent for leucine. When these data are subjected to statistical analysis,[29] it is found that the differences between preoperative and postoperative plasma levels are statistically significant for isoleucine, tryptophane, valine, methionine, threonine, arginine, phenylalanine, and lysine. Thus, the decreases in plasma levels following surgery are statistically insignificant only for leucine and histidine.

It does not appear that the decreases in plasma levels of the various individual essential amino acids can be attributed to plasma dilution. In the first place, there was little difference in mean hematocrit or mean serum albumin levels noted before and after surgery. In the second place, the work of Lyon and co-workers[20] in measuring plasma volume before and after surgery would seem to indicate that in the absence of shock or appreciable hemorrhage there is no noticeable change in plasma volume during surgery.

By the morning of the first postoperative day the mean plasma levels of seven of the ten individual essential amino acids were not statistically significantly different from the corresponding preoperative mean plasma levels. These amino acids were the following: leucine, isoleucine, tryptophane, valine, methionine, phenylalanine, and histidine. However, the mean plasma levels of threonine, arginine, and lysine were statistically significantly lower on the first postoperative day than the corresponding preoperative mean plasma levels. The mean plasma level of lysine returned to the preoperative level by the morning of the third postoperative day. The mean plasma levels of threonine and arginine did not, in this series, return to the corresponding preoperative mean plasma levels until the seventh postoperative day.

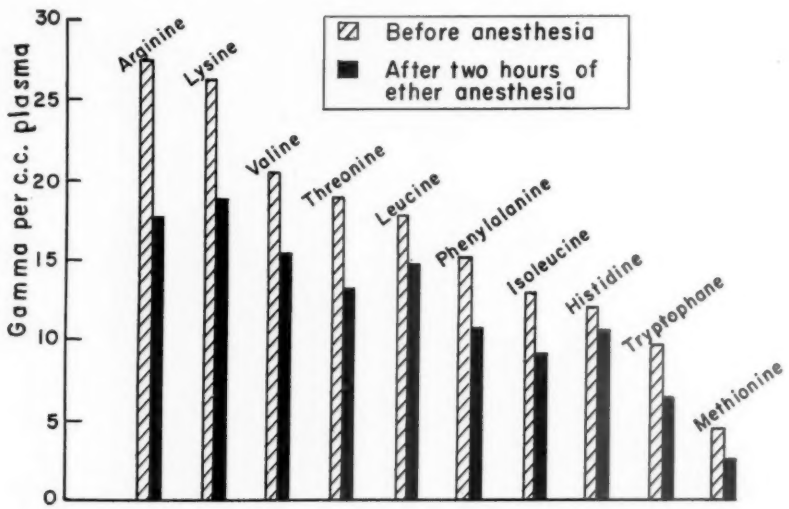

Fig. 3.—The effect of ether anesthesia on the individual essential (free) amino acids of plasma. (Average of ten dogs.)

There was no obvious relationship between the type and duration of anesthesia or the type and duration of operation and the amount of reduction of the various individual amino acids. Obviously, however, the series is small for comparisons of this nature.

Naturally, the question arose as to whether the lowering of the plasma amino acids might be due to the anesthesia alone and not the surgery. It was not thought justifiable to submit patients to several hours of additional anesthesia to establish this point. Consequently, ten dogs were subjected to two hours of ether anesthesia. Blood samples were drawn before and at the conclusion of the two-hour period of anesthesia. The plasma levels of the ten individual essential amino acids were determined in duplicate. Fig. 3 summarizes the data obtained in this study. Reference to Fig. 3 indicates that the ether anesthesia alone produces a lowering of the plasma levels of the individual essential amino acids equal to or greater than the depression of plasma level produced by anesthesia plus operation.

Although it seems likely that the depression of the plasma levels following surgery is caused by anesthesia, the question remains unanswered as to

the exact mechanism which produces the fall in plasma levels. Shock[13] and hemorrhage[27] are known to raise the plasma amino nitrogen level; consequently, they can largely be eliminated as responsible factors. That the change is part of the "alarm reaction" of Selye[28] seems unlikely since the work of Friedberg and Greenberg[8] and Li and co-workers[17] indicates that there is an increase in the level of plasma amino nitrogen following injection of cortical extract or adrenocorticotropic hormone. Injection of insulin has been demonstrated by Lotspeich,[18] by Harris and Harris,[9] and by us[6] to produce a lowering of the plasma individual amino acids. However, it is necessary to use doses of insulin sufficient to produce signs and symptoms of hypoglycemia in order to obtain decreases of the plasma levels comparable to those observed after surgery. Also, studies of the urinary excretion of the individual amino acids in five patients during surgery failed to demonstrate increased excretion of the amino acids sufficient to account for the depression of the plasma levels in the postoperative period.[6] The factor which on theoretical grounds conceivably might be responsible for the decreases in plasma levels of the amino acids following surgery is increased secretion of adrenalin. It is known that injections of adrenalin will produce lowering of plasma amino nitrogen.[3] Likewise, it is known that there is increased secretion of adrenalin during surgery or anesthesia.[24] Consequently, it is possible that the increased secretion of adrenalin is the factor responsible for the decrease in the plasma levels of the individual essential amino acids immediately after surgery or anesthesia.

SUMMARY

A study has been made of the effect of surgery on the plasma levels of the individual essential amino acids.

Following surgery the plasma levels of the individual essential amino acids decreased below the preoperative plasma levels. The plasma levels of seven of the ten essential amino acids returned to the preoperative level by the first postoperative day. Lysine returned to the preoperative plasma level by the third postoperative day. Threonine and arginine did not return to the preoperative mean plasma levels until the seventh postoperative day. Similar decreases in the plasma levels of the individual essential amino acids occurred following ether anesthesia without operation.

The decrease in plasma levels of the individual essential amino acids following surgery or anesthesia may possibly be due to the increased secretion of adrenalin which occurs during anesthesia or surgery. With the possible exception of arginine and threonine, decreases in plasma levels of the individual essential amino acids following surgery do not appear to be directly associated with the postoperative catabolic period.

REFERENCES

1. Browne, J. S. L., Schenker, V., and Stevenson, J. A. F.: Some Metabolic Aspects of Damage and Convalescence, J. Clin. Investigation **23**: 932, 1944.
2. Brunschwig, A., Clark, D. E., and Corbin, N.: Post-Operative Nitrogen Loss and Studies on Parenteral Nitrogen Nutrition by Means of Casein Digest, Ann. Surg. **115**: 1091-1102, 1942.

3. Crismon, C. A., Hanvey, R. V., and Luck, J. M.: Effects of Epinephrine, Potassium, Pentobarbital and Insulin on Concentration of Amino Acid Nitrogen in Blood of Fasting Dogs, Am. J. Physiol. **130:** 171-176, 1940.
4. Cuthbertson, D. P.: Observations on the Disturbance of Metabolism Produced by Injury to the Limbs, Quart. J. Med. **25:** 233-246, 1932.
5. Cuthbertson, D. P.: Post-Shock Metabolic Response, Lancet **1:** 433-436, 1942.
6. Everson, T. C., and Fritschel, M. J.: Unpublished data.
7. Farr, L. E., MacFadyen, D. A., Taylor, G., Shands, A. R., Jr., Ferguson, W. R., Dunlap, E. B., Jr., and Johnson, C.: Changes in Plasma Amino Acid Nitrogen Concentration Following Nitrous Oxide and Ether Anesthesia and Surgery, Proc. Soc. Exper. Biol. & Med. **50:** 256-258, 1942.
8. Friedberg, F., and Greenberg, D. M.: Endocrine Regulation of Amino Acid Levels in Blood and Tissues, J. Biol. Chem. **168:** 405-409, 1947.
9. Harris, M. M., and Harris, R. S.: Effect of Insulin Hypoglycemia and Glucose on Various Amino Acids in Blood of Mental Patients, Proc. Soc. Exper. Biol. & Med. **64:** 471-476, 1947.
10. Hier, S. W., and Bergeim, O.: Microbiological Determination of Free Leucine, Isoleucine, Valine, and Threonine in Dog Plasma, J. Biol. Chem. **161:** 717-722, 1945.
11. Hier, S. W., and Bergeim, O.: Microbiological Determination of Certain Free Amino Acids in Human and Dog Plasma, J. Biol. Chem. **163:** 129-135, 1945.
12. Hier, S. W.: Thesis: Studies on the Free Amino Acids of Blood and Sweat, University of Illinois, 1947.
13. Hoar, W. S., and Haist, R. E.: Amino Acid Nitrogen Changes in Shock, J. Biol. Chem. **154:** 331-338, 1944.
14. Hoffman, W. S.: Photelometric Clinical Chemistry, New York, 1941, William Moran & Co.
15. Howard, J. E., Parson, W., Stein, K. E., Eisenberg, H., and Reidt, V.: Nitrogen Metabolism After Fracture and Skeletal Operations in Healthy Males, Bull. Johns Hopkins Hosp. **75:** 156-168, 1944.
16. Kline, D. L.: The Effect of Hemorrhage on the Plasma Amino Nitrogen of the Dog, Am. J. Physiol. **146:** 654-663, 1946.
17. Li, C. H., Geschwind, I., and Evans, H. M.: The Effect of Growth and Adrenocorticotropic Hormones on the Amino Acid Levels in Plasma, J. Biol. Chem. **177:** 91-95, 1949.
18. Lotspeich, W. D.: The Role of Insulin in the Metabolism of Amino Acids, J. Biol. Chem. **179:** 175-180, 1949.
19. Lürje, A.: Protein Metabolism Disturbances Under Conditions of Shock and Surgical Interference, Am. J. Surg. **32:** 313-317, 1936.
20. Lyon, R. P., Stanton, J. R., Freis, E. D., and Smithwick, R. H.: Blood and "Available Fluid" (Thiocyanate) Volume Studies in Surgical Patients: I. Normal Patterns of Response of the Blood Volume, Available Fluid, Protein, Chloride and Hematocrit in the Postoperative Surgical Patient, Surg., Gynec. & Obst. **89:** 9-19, 1949.
21. Man, E. B., Bettcher, P. G., Cameron, C. M., and Peters, J. P.: Plasma Alpha Amino Acid Nitrogen and Serum Lipids of Surgical Patients, J. Clin. Investigation **25:** 701-708, 1946.
22. Man, E. B., Bettcher, P. G., Cameron, C. M., and Brown, W. T.: Plasma Alpha Amino Acids, Serum Lipids, and Proteins After Prefrontal Lobotomy in Seven Schizophrenic Patients, Yale J. Biol. & Med. **20:** 175-183, 1947.
23. Munro, H. N., and Cumming, M. C.: Nitrogen Metabolism After Fracture, Nature **161:** 560-561, 1948.
24. Pekkarinen, A.: Studies on the Chemical Determination, Occurrence and Metabolism of Adrenalin in the Animal Organism, Acta physiol. scandinav. supp. **54:** 5-11, 1948.
25. Peters, J. P., and Man, E. B.: Some Metabolic Reactions to Injury, Tr. A. Am. Physicians **59:** 237-241, 1946.
26. Rose, W. C.: Amino Acid Requirements of Man, Federation Proc. **8:** 546-552, 1949.
27. Sayers, M. A., Sayers, G., Engel, M. G., Engel, F. L., and Long, C. N. H.: Elevation of Plasma Amino Nitrogen as an Index of the Gravity of Hemorrhagic Shock, Proc. Soc. Exper. Biol. & Med. **60:** 20-22, 1945.
28. Selye, H.: General Adaptation Syndrome and Diseases of Adaptation, J. Clin. Endocrinol. **6:** 117-230, 1946.
29. Snedecor, G. W.: Statistical Methods Applied to Experiments in Agriculture and Biology, ed. 4, Ames, 1946, The Collegiate Press, Inc.

EXPERIMENTAL AND CLINICAL OBSERVATIONS ON INTRAVENTRICULAR AND INTRACEREBRAL INJECTION OF BACITRACIN

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IN ORDER to test the toxicity of bacitracin by direct application to the central nervous system, this antibiotic was injected into the right lateral ventricle of 10 cats.

METHOD

Ten normal adult cats weighing from 2 to 2.85 kilograms were used in this experiment. The head of the experimental animal was shaved and the scalp was prepared with iodine and alcohol. The operating field was draped with sterile towels when the animal was lightly anesthetized. Five cats were given ether by inhalation and 5 were anesthetized by the intravenous injection of Nembutal, 30 mg. per kilogram of body weight. A right parasagittal scalp incision, 2 inches long was made and the periosteum as well as the temporal muscle was separated from the underlying skull by means of a periosteal elevator. A ½-inch burr hole was drilled in the anterior part of the skull and the opening was further enlarged to 1 by ¾ inch with a small rongeur. The dural flap was reflected medially. The sulcus cruciatus, sulcus ansatus, sulcus suprasylvius anterior, and the sulcus lateralis were identified. A hypodermic needle was lowered perpendicularly into the right cerebral hemisphere at the point 1 cm. posterior to the sulcus ansatus and 0.5 cm. lateral to the midline (Fig. 1). At a depth of about 1 to 1.2 cm. the needle entered the lateral ventricle into which 5,000 units of bacitracin in 0.5 c.c. of physiologic saline solution were delivered from a tuberculin syringe in from 2 to 3 seconds. The wound was closed in layers with silk.

OBSERVATION

After the intraventricular instillation of bacitracin, each animal was observed for 2 to 3 hours before it was sent back to the animal cage.

Of the 5 animals observed under intravenous Nembutal anesthesia, 3 developed muscular twitchings involving the neck and all the limbs starting 10 minutes after the intraventricular injection of 5,000 units of bacitracin, and lasting from 35 to 55 minutes. There were no generalized convulsions.

Two cats developed generalized convulsions 10 minutes after the intraventricular injection. Nevertheless, each animal had only 1 seizure which lasted 30 to 45 seconds.

The bacitracin used was supplied by the Commercial Solvents Corporation of Terre Haute, Indiana.

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All 5 animals survived the injection and the surgical procedure except for one which died on the third postoperative day from a wound infection. Direct smear of the discharge from the wound revealed a Gram-negative bacillus. Autopsy disclosed a generalized meningitis. Frank pus was seen in the cerebral subarachnoid space, more in the basal cisterns and about the site of operation. Culture was not taken. Other viscera looked normal. The brain specimen of this animal was not preserved.

In order to eliminate the anticonvulsive effect of the Nembutal, 5 cats were operated upon under light ether inhalation. Each animal was allowed to wake up from the anesthesia before the intraventricular injection of bacitracin. Therefore, the wound was closed without anesthesia.

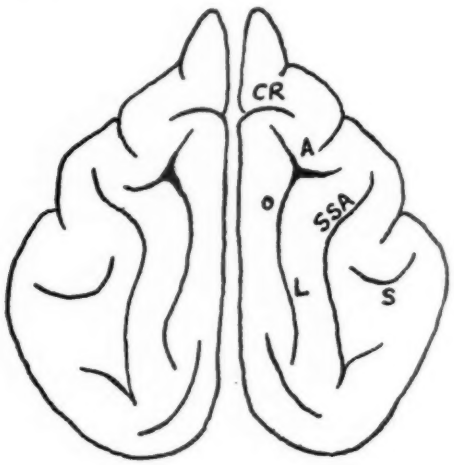

Fig. 1.—Topography of cat's brain. *O* indicates the site of injection; *CR*, sulcus cruciatus; *A*, sulcus ancatus; *SSA*, sulcus suprasylvius anterior; *L*, sulcus lateralis; and *S*, sulcus pseudosylvius.

All of the 5 animals developed a series of generalized convulsions which appeared from 9 to 14 minutes after the intraventricular instillation of bacitracin. Two cats were unconscious during the seizures and did not react to painful stimuli, while 3 had no disturbance of consciousness. They struggled to sit on their legs between seizures. The number of seizures in each animal varied from 7 to 12 and each convulsion lasted from 5 to 45 seconds. The last convulsion in each of these animals occurred from 50 to 70 minutes after the first seizure. All animals survived the convulsions, but 1 died 24 hours later from "distemper" with profuse nasal discharge and pneumonic consolidation of lungs. The brain specimen of this animal was discarded.

All of the 8 surviving animals were sacrificed at the end of 1 month during which time there was no sign of disability that could be elicited. All were killed by giving intravenous Nembutal and a complete autopsy was performed in each animal. The findings were essentially normal as indicated below.

Gross Pathology.—All of the cats showed well-healed scars in the scalp and in the dura at the site of the operation. In 3 instances the dura was found to be adherent to the cortex at the site of the incision in the dura. The me-

ninges remote from the area of operation showed no evidence of thickening. The needle tract was found in the cross section of every specimen. However, no evidence of a needle puncture could be located in the corpus callosum in 2 of the 8 brains. Probably the injection was intracerebral. These 2 animals were injected under Nembutal anesthesia. One developed a generalized convulsion 10 minutes after the injection, lasting 45 seconds, and the other had no convulsion but a generalized muscular twitching which lasted 16 minutes, 10 minutes after the intracerebral injection of bacitracin. The brains of these 2 animals and one of the others with an intraventricular injection of bacitracin showed a small area of hemorrhage around the needle tract. Otherwise, the cerebral and the cerebellar cortex, the ventricular surface, and the chorioid plexus of all specimens looked normal.

Section of the kidneys revealed no gross pathology.

Microscopic Examination.—The cerebrum was sectioned along its coronal plane and the sections were stained with Nissl's methylene blue and hematoxylin-eosin. A few lymphocytes were seen in the subarachnoid space and occasionally they infiltrated the arachnoid membrane which was slightly thickened in the area of operation. The dura and the arachnoid remote from the site of operation were normal. There was a small area of softening in the white matter of the cerebrum with minimal glial-cell reaction neighboring the needle tract. In three specimens, minimal hemorrhage was seen amid the area of softening (Figs. 2 and 3). Sections of Nissl's stain demonstrated no evidence of degeneration of the cortical neurons even in the area through which bacitracin had been instilled. The chorioid plexus and the ependymal lining of the ventricles looked normal in every specimen.

Comment.—This experiment shows that the intraventricular or intracerebral injection of 5,000 units of bacitracin in ½ c.c. of normal saline solution to cats of 2 to 2.85 kilograms of body weight caused transient seizures. Of the 5 animals which were injected under Nembutal anesthesia, 2 developed a single generalized convulsion and 3 exhibited only muscular twitchings. Repeated attacks of jacksonian seizures lasting 50 to 70 minutes were observed in all of the other 5 cats injected under ether anesthesia. Nevertheless, all 10 animals survived the injection although 2 died from postoperative complications. Five thousand units of bacitracin for a cat weighing 2 kilograms would correspond to 175,000 units for a 70 kilogram man by the intraventricular route. Probably 100,000 units of bacitracin could be given into the ventricle of an adult patient without causing untoward effects, but for the present a limit of 50,000 units at any one time is recommended. We have employed this dosage in 5 c.c. of normal saline solution by intracranial instillation without observing any toxic effect.

Other Experimental Observations.—Walker and Johnson demonstrated that approximately 500 units of penicillin injected into the ventricular system or by topical application to the cerebral cortex in dogs and monkeys caused epileptic manifestations.[1] The intracortical instillation of 1,000 units of peni-

cillin in both cats and monkeys induced myoclonic jerkings.[2] They also pointed out that in human beings, penicillin applied to the cortex in doses of 10,000 to 20,000 units may produce convulsions.

CLINICAL OBSERVATIONS

We have applied 10,000 to 50,000 units of bacitracin in a concentration of 2,500 to 10,000 units per c.c. in normal saline solution to 45 patients[5, 6] not only to an intact cortical surface but also to the cut surface after topectomy or lobectomy without producing any signs of cerebral irritation. Repeated injections by the intraventricular route in a dosage varying from 3,000 to 50,000

Fig. 2.

Fig. 3.

Fig. 2.—Section of brain, cat No. 840. Hematoxylin-eosin stain. Shows the area of hemorrhage, softening, and minimal glial reaction at the site of intracerebral injection of 5,000 units of bacitracin in ½ c.c. of normal saline solution. Animal killed 1 month after the test. (×75.)

Fig. 3.—Section of brain, cat No. 841. Nissl's stain. Shows the same change along the needle tract as in Fig 2, 1 month after the intraventricular injection of 5,000 units of bacitracin in ½ c.c. of normal saline solution. (×100.)

units of bacitracin have been given to 8 patients in the treatment of infections or for postoperative prophylaxis, and have produced no irritative symptoms.[3, 4, 5] One further illustrative case is presented below.

CASE REPORT

B. E., a 63-year-old man, was admitted to the Mount Sinai Hospital on June 16, 1949, and 5 days later an ependymoma was removed from the right lateral ventricle through a right sided Frazier bone flap. The postoperative course was uneventful until the fifth day after

the operation, when the temperature rose to 104° F. and the neck became rigid. A ventricular puncture yielded 15 c.c. of cloudy sanguinous fluid. Infection being suspected, although direct smear and culture of this fluid revealed no microorganism, 10,000 units of bacitracin in 10 c.c. of normal saline solution were instilled into the right lateral ventricle. From beneath the scalp through the operative wound 20 c.c. of cloudy bloody fluid were aspirated, and 10,000 units of bacitracin in 1 c.c. of normal saline solution were delivered into the subgaleal space. Into the lumbar subarachnoid space the same amount of bacitracin was injected after 10 c.c. of turbid cerebrospinal fluid had been removed. Supplementary bacitracin, 10,000 units every 6 hours, and procaine penicillin, 600,000 units every 6 hours, were given by the intramuscular route. The former antibiotic was stopped after the second intramuscular dose, and the latter was continued for 10 days. The patient was alert and took fluid by mouth. The temperature became normal on the second day of this treatment. The wound healed without any signs of suppuration. Cultures of the ventricular, the spinal, and the subgaleal fluid all showed no growth.

TABLE I. THE INJECTION OF 5,000 UNITS OF BACITRACIN IN 0.5 C.C. OF NORMAL SALINE SOLUTION INTO THE RIGHT LATERAL VENTRICLE IN THE CAT

ANIMAL NO.	ANESTHESIA	BODY WEIGHT (IN KG.)	RESULT
817	Nembutal	2.0	1 generalized convulsion, 10 minutes after the intraventricular injection; seizure lasted 30 seconds; no loss of consciousness during seizure; recovery complete; no paralysis
840	Nembutal	2.4	1 generalized convulsion, 10 minutes after the injection, later found to be intracerebral; seizure lasted 45 seconds; no paralysis; complete recovery
842	Nembutal	2.2	Muscular twitchings of trunk and limbs; no generalized convulsion; complete recovery
856	Nembutal	2.85	No convulsion; muscular twitchings appeared 10 minutes after injection, later found to be intracerebral; complete recovery; no paralysis
857	Nembutal	2.1	No convulsion; muscular twitchings, limbs and trunk; died from wound infection and meningitis, 3rd day (Gram-negative bacillus)
408	Ether	2.6	Muscular twitchings and 10 generalized convulsions, each lasted 15 to 30 seconds; seizures set in 9 minutes after the injection lasting over a period of 52 minutes; recovered
835	Ether	2.0	7 generalized convulsions appeared 10 minutes after the injection; each lasted 5 to 20 seconds; no loss of consciousness during seizures lasting over a period of 60 minutes; complete recovery
841	Ether	2.5	12 convulsions, 10 minutes after injection; complete recovery; each seizure lasted 30 to 45 seconds, lasting over a period of 70 minutes; no loss of consciousness
843	Ether	2.1	7 convulsions, generalized; each lasted 17 to 35 seconds, lasting over a period of 50 minutes; died from distemper 2 days later
616	Ether	2.25	10 seizures, generalized, 12 minutes after the injection; each lasted 10 to 20 seconds; no loss of consciousness during convulsions; complete recovery; convulsions lasted over a period of 66 minutes

Comment.—In the case described above there was no bacteriologic evidence of infection. The symptoms were probably caused by bleeding from the lateral wall of the ventricle from which the tumor had been removed. The case demonstrates that bacitracin may be given by the intraventricular and intrathecal routes and into the scalp wound as a prophylactic, without any evidence of local irritation or systemic toxicity.

During the early commercial production of bacitracin by the deep-tank method certain lots showed a disturbing degree of kidney irritation. Our clinical data have shown that when bacitracin was injected into the intracranial cavity or the subarachnoid space alone, without any intramuscular administration, there were no urinary or renal changes. When local treatment to the central nervous system was fortified by intramuscular injections of bacitracin in doses of 10,000 to 20,000 units at intervals of 4, 6, or 8 hours, transient albuminuria and cylindruria may appear but they usually disappear during treatment or soon after treatment has been stopped. No significant rise in blood urea nitrogen has been observed in our series of cases.[5]

SUMMARY

1. Five thousand units of bacitracin in ½ c.c. of normal saline solution were injected into the right lateral ventricle through a craniotomy wound in 10 cats, 5 under Nembutal and 5 under light ether anesthesia.

2. Seven to 12 convulsive seizures lasting from 50 to 70 minutes occurred after the intraventricular injection of bacitracin in the 5 cats which were operated upon under light ether anesthesia. In the other 5 animals given Nembutal anesthesia, 2 developed one generalized seizure while 3 exhibited only muscular twitchings of the limbs and the trunk. In 2 of the last group of animals in which the injection was probably intracerebral, one developed a generalized convulsion and the other had only muscular twitchings.

3. All animals survived the injection and the convulsive manifestation. Two cats died from postoperative complications. The survivals showed no signs of disability.

4. All surviving cats were killed 1 month after the intraventricular instillation of bacitracin. Pathologic examination of the brain revealed minimal glial-cell reaction, small areas of softening in the white matter of the cerebral hemisphere and minimal amounts of bleeding in the softened area at the site of injection. The arachnoid membrane was thickened only in the exposed area of operation.

5. Bacitracin has been used in the treatment of infections involving the central nervous system in patients and no ill effects have been observed. Its clinical use by the intraventricular and intracerebral routes is to be recommended. One illustrative case is presented.

REFERENCES

1. Walker, A. E., and Johnson, H. C.: Principles and Practice of Penicillin Therapy in Diseases of the Nervous System, Ann. Surg. **122**: 1125-1135, 1945.
2. Walker, A. E., and Johnson, H. C.: Convulsive Factor in Commercial Penicillin, Arch. Surg. **50**: 69-73, 1945.
3. Teng, P, and Meleney, F. L.: The Treatment of Staphylococcic Meningitis; With a Review of the Literature and With Particular Reference to the Results With Bacitracin: A Report of 5 Cases, SURGERY **28**: 516-533, 1950.
4. Teng, P.: Further Experiences in the Treatment of Septic Meningitis With Bacitracin, Arch Neurol. & Psychiat. **64**: 861-877, 1950.
5. Teng, P., Cohen, I., and Meleney, F. L.: Bacitracin in Neurosurgical Infections, Surg., Gynec. & Obst. **92**: 53-63, 1951.
6. Teng, P.: Unpublished data.

ONE-STAGE RECONSTRUCTION OF THE CERVICAL ESOPHAGUS OR TRACHEA

MILTON THOMAS EDGERTON, M.D.,* BALTIMORE, MD.

IT IS now possible in many cases to carry out immediate reconstruction of the oral cavity or upper pharynx at the time of surgical excision of malignant or radionecrotic ulcers. This has resulted in a tremendous reduction in length of hospitalization and postoperative morbidity for this group of patients. In the majority of cases, only the floor of the mouth or one wall of the pharynx need be removed, and under these circumstances a previously delayed local cervical skin flap may be used for immediate reconstruction.

However, with bulky carcinomas of the extrinsic larynx or hypopharynx, with some carcinomas of the base of the tongue, and with carcinoma of the cervical esophagus, it is usually necessary to remove all or at least the greater part of the circumference of the lower pharynx and cervical esophagus.

The larynx must be removed in most such cases, and a permanent tracheostomy is usually employed. In this manner the surgeon has a moderately satisfactory solution to the problem of the upper respiratory tract. However, at the same time, the requirements of the gastrointestinal tract make it imperative that some method be found whereby food and the salivary and mucous gland secretions from the oral and nasal cavities may be conveyed to the stomach. It is important that the patient be spared the problems of a permanent gastrostomy, that he be enabled to taste properly, and to take his meals in normal fashion. It may thus be seen that some method of early reconstruction of the cervical esophagus would be desirable.

BACKGROUND

The recent return to the more extensive use of radical surgery in the treatment of certain head and neck tumors has given the plastic procedure of Harold Wookey acceptability in many clinics. Our experience in the use of this method has been rather disappointing. In the first place many of these patients are malnourished when first seen, and tolerate poorly the long periods of hospitalization and abnormal feeding. Secondly, the Wookey procedure requires extensive and diligent nursing care for several weeks to prevent constant salivary secretion from entering the newly established tracheostomy (Fig. 1).

The report of Rob and Bateman in October, 1949, described the use of a cylinder of tantalum gauze applied to defects in the cervical region of both the trachea and the esophagus. They covered the tantalum inside and out with fascia lata. The fascia was used primarily with the idea of establishing a "temporary seal during the first few hours to limit infection while the tissue planes are being closed off." The tantalum was simply used as a splint to prevent stenosis. However, in several of the cases reported the necrotic fascia

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had to be picked out on pharyngoscopy in the early postoperative period, and there was also some difficulty with obstruction of the lumen. In our use of fascia lata in other parts of the body, we have found it a material highly vulnerable to infection when used as a free graft. Like tendon it is almost avascular. Thus to expose it to the secretions of the oral cavity would seem to invite the infection and necrosis which in fact occurred in the reported cases. On the other hand, split-thickness skin grafts have proved highly resistant to

Fig. 1.—This patient, G. S., a 58-year-old plumber with carcinoma of the hypopharynx, was treated by a modification of the Wookey operation and shows some of the difficulties encountered in postoperative management. The saliva drains down from the opening into the pharynx and has a tendency to get into the newly formed tracheostomy. Usually four to five weeks are required before the cervical skin flap can be turned back on itself to reconstruct the esophagus. The skin from the submaxillary region in this patient was turned up to reconstruct the upper portion of the pharynx because of the very high resection required here.

infection and take well, not only in the oral cavity but even in saucerized defects within osteomyelitic bone. In addition, such skin grafts come to simulate rather closely the normal lining of the pharynx and upper esophagus, apparently undergoing some metaplasia with a decrease in the amount of keratin. Accordingly, it seems that skin may be superior to fascia in effecting a seal

while at the same time serving as a permanent substitute for the excised mucosa. It should be noted that if this concept is accurate, one need not leave a small strip of the original mucosa, as Rob and Bateman did.

While it is recognized that the epithelial linings of both the esophagus and the trachea have an unusual ability to regenerate, it is often true that this regeneration is accompanied by a varying degree of stenosis. It would seem important to replace large defects in the surface of epithelial tubes within the body by epithelial grafts just as in the case of similar defects on the outside body surface.

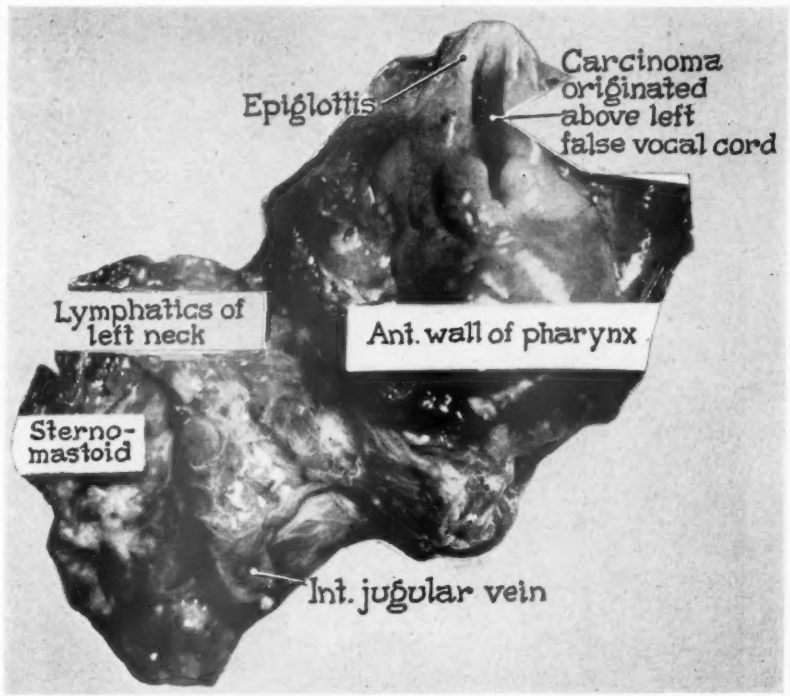


Fig. 2, *A* (Case 1).—W. C., a 34-year-old Negro laborer admitted to The Johns Hopkins Hospital with eight months' history of hoarseness. Specimen removed in continuity with lymphatics of left neck, including the wall of the pharynx and a total laryngectomy for carcinoma of the extrinsic larynx.

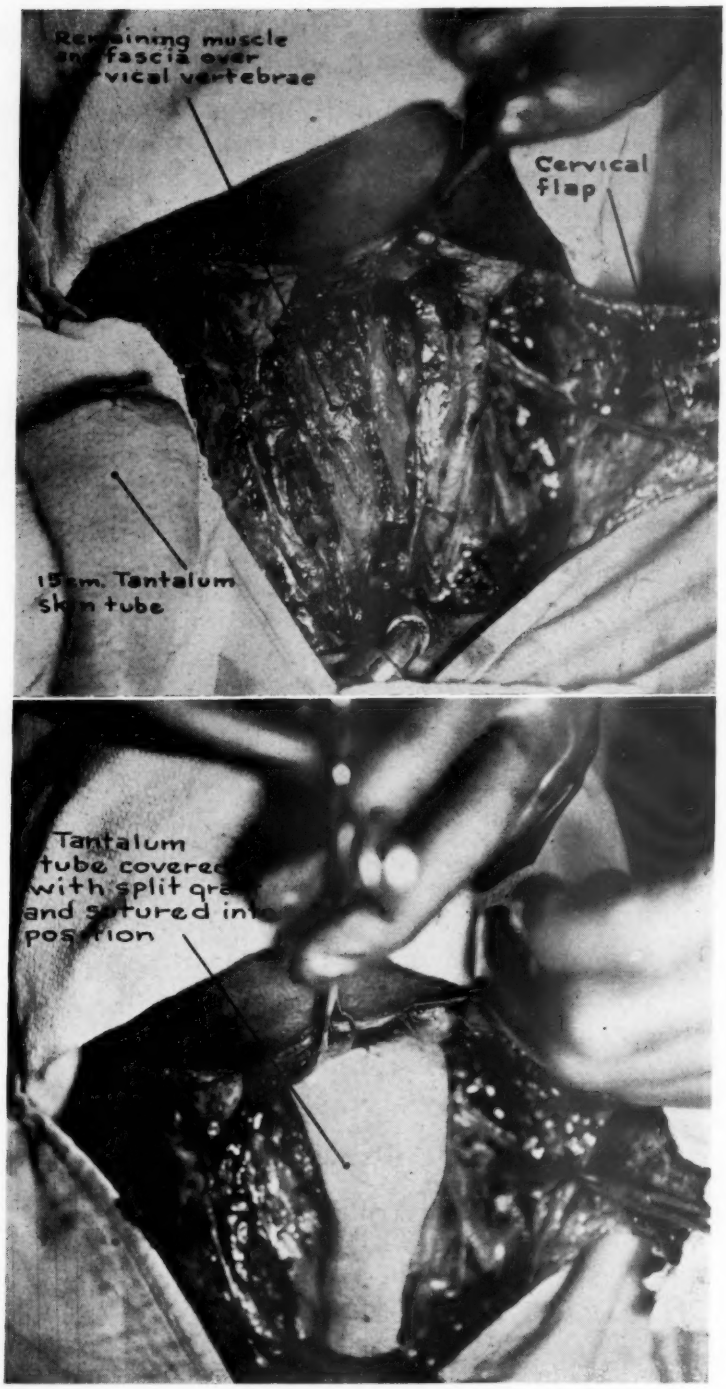
METHOD

The plastic surgical service has treated four patients in whom free skin grafts were used in conjunction with a metal mesh splint to repair segmental defects in the esophagus and pharynx.* The first of these was a young Negro man of thirty-four with a large squamous carcinoma of the extrinsic larynx (Fig. 2, *A-F*). This had invaded the left pyriform sinus and extended down 3 cm. into the cervical esophagus. There was marked deformity of the epiglottis with definite stridor.

A large rectangular flap was elevated from the anterior neck with its pedicle placed laterally to the left (Fig. 2, *C*). The larynx was resected en

*Since submission of this paper three additional cases have been treated with this technique with similar satisfying results.

B.



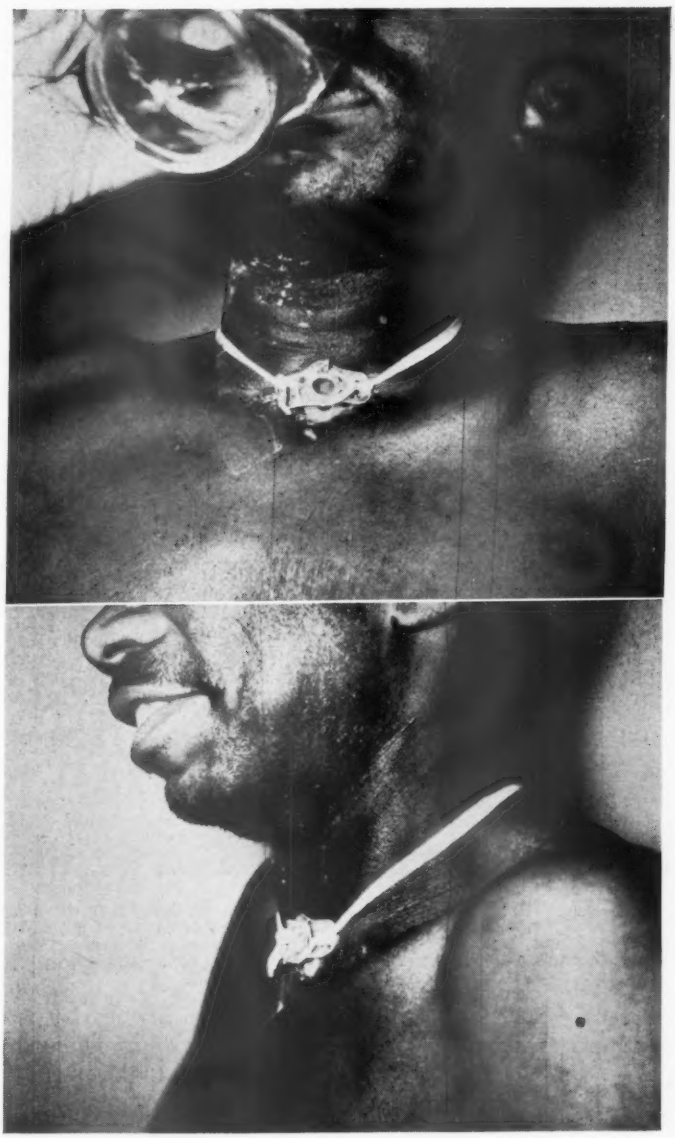
C.

Fig. 2, *B* (Case 1).—Defect in cervical region at time of operation. All the tissues have been removed down to the muscles of the cervical vertebrae. The common carotid and internal carotid arteries were left, but it was necessary to remove the hyoid bone and the base of the tongue to get adequate margin around the growth. On the left may be seen the segment of esophagus and pharynx about to be inserted.

C, This 14 cm. segment of tantalum gauze has now been shaped into a truncated cone with a wide circumference at the top exactly matching that of the transected pharynx. A three-quarter-thickness split-skin graft taken from the thigh has been sutured around this tantalum with the "raw surface" facing the surrounding tissues of the neck.

bloc, together with the upper two rings of the trachea, the upper esophagus, lower pharynx, hyoid bone and base of tongue, and a radical neck dissection was performed on the left side. The strap muscles and left lobe of the thyroid were included in the block. A fine mesh tantalum gauze was then fashioned into a truncated cone 15 cm. long so that the smaller end would just fit into the distal segment of the esophagus. The larger proximal end was approximately equal in diameter to the pharynx just below the level of the tonsils. A three-

D.



E.

Fig. 2, *D* (Case 1).—Shows patient three weeks following removal of tumor, now able to take full liquid diet without evidence of fistula.

E, Shows patient having gained twenty-two pounds in the first six weeks following surgery. He has developed a very satisfactory esophageal voice.

quarter-thickness split-skin graft was then taken from the left thigh and applied about the outer surface of the tantalum cone with the epidermal side facing the lumen and the subcuticular surface facing the surrounding tissues of the neck. Care was taken to allow the graft to extend about 1 cm. beyond the limits of the tantalum. This sleeve of graft was turned down within the mesh so as to cover the sharp metal edges. The graft was fixed in place about the cone, with a number of 0000 chromic catgut sutures. The distal end of the

Fig. 2, *F* (Case 1).—Barium swallow taken eight weeks after insertion of skin graft and tantalum mesh. This represents two separate roentgenograms of pharynx and lower neck taken simultaneously. There is very rapid passage of barium through reconstructed segment. Note the bending of the metallic mesh in the lower portion, secondary to pressure from the tracheotomy tube.

cone was then inserted about 2 cm. within the esophagus, and the esophagus was then anastomosed to the cone by means of additional interrupted catgut sutures. At the upper end a simple end-on anastomosis was employed in order to minimize any leakage of saliva into the deep cervical tissues. A Levine tube was passed through the newly made segment into the stomach for postoperative feeding. The skin flap, raised on the neck at the beginning of the operation, was then laid back across the anterior surface of the tantalum tube, care being

taken to see that it lay in close contact with the lateral and ventral surfaces of the split-thickness graft surrounding the tantalum. The remaining portion of the trachea was then sutured to the skin in the suprasternal region as a permanent tracheostomy. Two small Penrose drains were brought out beneath the lower border of the flap. A firm cotton waste dressing was then applied about the neck.

Postoperative Course.—Pathologic report revealed a poorly differentiated squamous carcinoma originating in the larynx, with extension locally, but metastasis found in only one deep cervical lymph node. On the fifteenth postoperative day the patient was able to take a liquid diet by mouth. There was no fistula. The drains were removed on the sixth postoperative day and there was no evidence of abscess formation or severe febrile response. We were concerned about the ability of this patient to swallow because of the removal of hyoid bone and base portion of tongue. However, he swallowed quite easily from the first and continues to do so. The patient gained twenty-two pounds within the next four weeks, and has developed a very adequate esophageal voice. After operation, in spite of the absence of the constrictor muscles of the pharynx, barium swallow revealed only a very slight delay at the lower end of the reconstructed segment. In the weeks following operation the tantalum was examined endoscopically on several occasions. There seemed to be no tendency of the cervical tissues to grow up through the mesh. About four months postoperatively the patient complained of a stiff feeling in his neck on extreme motions of his head. Under a light Pentothal sodium anesthesia, the mesh was firmly grasped with a pair of forceps passed through a bronchoscope and, with strong traction, was readily removed through the mouth. The skin graft was seen to have taken nicely and the esophagus had an adequate lumen and a pink healthy color. The patient subsequently noted some further improvement in the ease of swallowing and eight months after operation took a full diet without difficulty. It is interesting that these patients can swallow even when lying supine.

This combination of skin graft and metallic mesh has been used in three other patients. Case 2 (J. C.) was a 56-year-old man with a squamous carcinoma of the pharyngoepiglottic fold (Fig. 3, *A-C*). The treatment employed was essentially the same as in the first case except that it was unnecessary to remove the entire circumference of the esophagus. A narrow strip of mucosa 1 cm. wide was left on the posterior wall. The retention of this mucosa is apparently not essential for preservation of the swallowing mechanism but it would appear that it might tend to help prevent stricture formation. Thus far postoperative dilatation has not been required. On this second patient the fine mesh used was of stainless steel rather than tantalum. This change was made in the interest of providing a stronger form or stent for the skin graft. The steel is made in a closer weave and is correspondingly stiffer than the tantalum, thus permitting a firmer pressure dressing without risking compression of the tube. Seven months postoperatively the patient was eating well and was without recurrence.

The third patient (Case 3) entered with a smaller carcinoma lying in the right pyriform sinus. A composite resection was carried out removing valleculae and lateral pharyngeal wall. A direct approximation of the edges of the defect would have produced serious binding of the tongue to the palate. To meet this problem a circular piece of steel mesh gauze was fitted to the defect. Again a split-thickness graft was applied over this so that the epidermal side faced the pharyngeal lumen through the spaces of the mesh. The elevated cervical flap was then simply dressed against the "raw" side of the graft. After two weeks the mesh was readily removed through the mouth and revealed a satisfactory take of the graft. Four months later the patient was still free of recurrence and although the right mandible was replaced with a steel bar he is able to eat quite well.

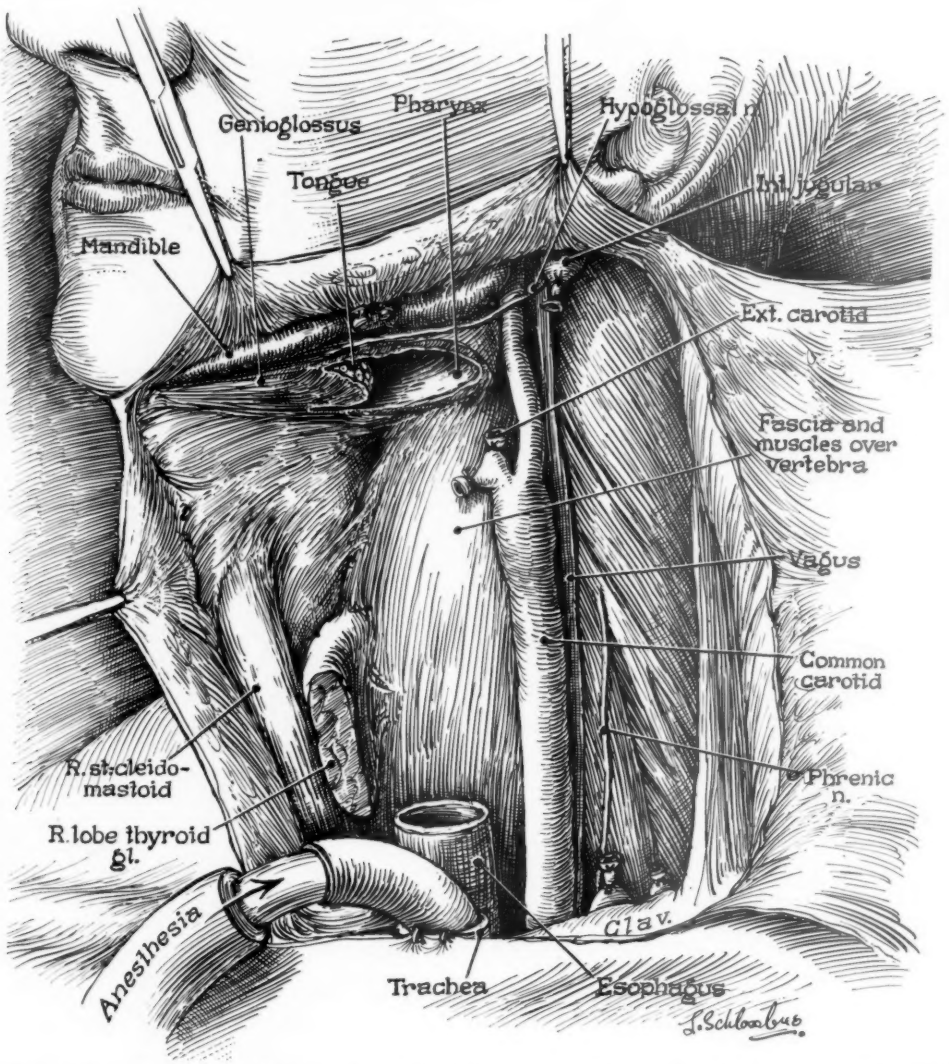


Fig. 3, *A*.—Sketch showing the remaining structures of deep neck after removal of specimen, containing tumor. In many cases it is possible to leave a tiny strip of uninvolved pharyngeal mucosa on posterior wall. This is not necessary but probably aids in re-establishing the swallowing mechanism. At least one lobe of the thyroid should be preserved along with associated parathyroids. If the growth is small and low-lying the hyoid bone and base of tongue sometimes may be preserved.

A fourth patient (G. M.), a 62-year-old white man (Fig. 3, *A-C*) also had a complete resection of a 12 cm. segment of pharynx and esophagus for an anaplastic carcinoma of the upper esophagus and lower pharynx. Once more a laryngectomy, tracheostomy, and reconstruction of esophagus with steel mesh and skin graft were carried out. Although the growth appeared to be removed locally, pathologic examination showed a tumor thrombus in the left facial vein and the prognosis is probably poor. This patient was treated recently but is reported because he is the first patient to show some necrosis of the edge of his skin flap. This exposed a 2 cm. area of mesh and the fistula required a chest flap for closure. This fistula was simply closed as it involved only the anterior wall of the esophagus. The patient is now without pain or recurrence. He is eating a full diet and has gained fourteen pounds.

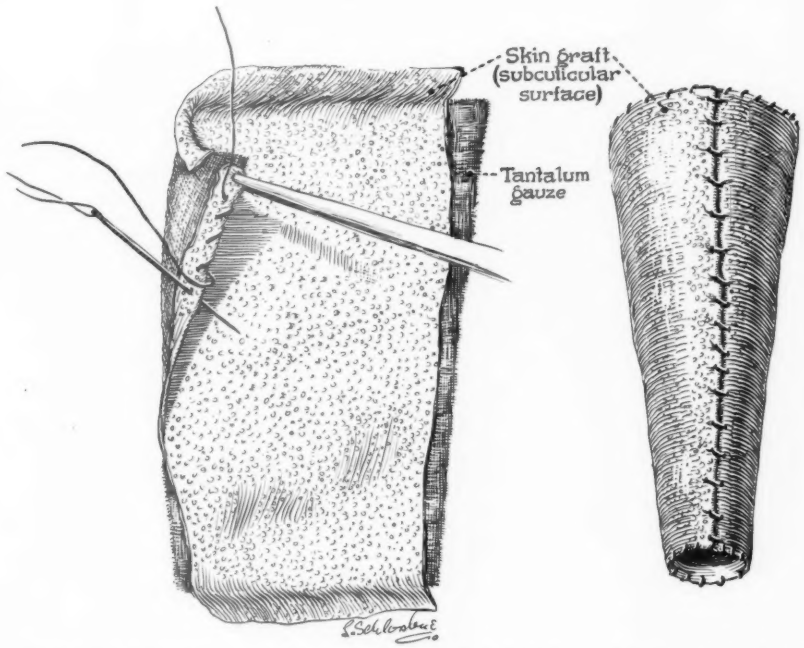


Fig. 3, *B*.—Sketch of tantalum or stainless steel mesh being formed into a cone to support the free graft.

The transverse cervical flaps are quite long and should be designed to reach well across the midline. If there is node involvement, requiring a radical neck dissection, it would probably be best to base the flap on the uninvolved side of the neck, or perhaps carry out a preliminary "delay" operation.

APPLICATION TO TRACHEAL DEFECTS

Ronald Belsey reported in October, 1950, the use of fascia lata around a special coiled spring to repair a defect of the trachea. He reasoned that the coil would give some longitudinal elasticity to the reconstructed segment and again pointed out that in the trachea, unlike the esophagus, permanent lateral rigidity is required. In Belsey's patient it was necessary to reopen the chest and use living pulmonary tissue to control an air leak. Belsey also noted the

development of a stricture of the tracheal lumen to about one-half of its caliber within one year. Longitudinal elasticity is probably not necessary in reconstruction unless a very long segment of trachea is removed. It also seemed possible that the use of a skin graft might serve to eliminate a continuing air leak post-

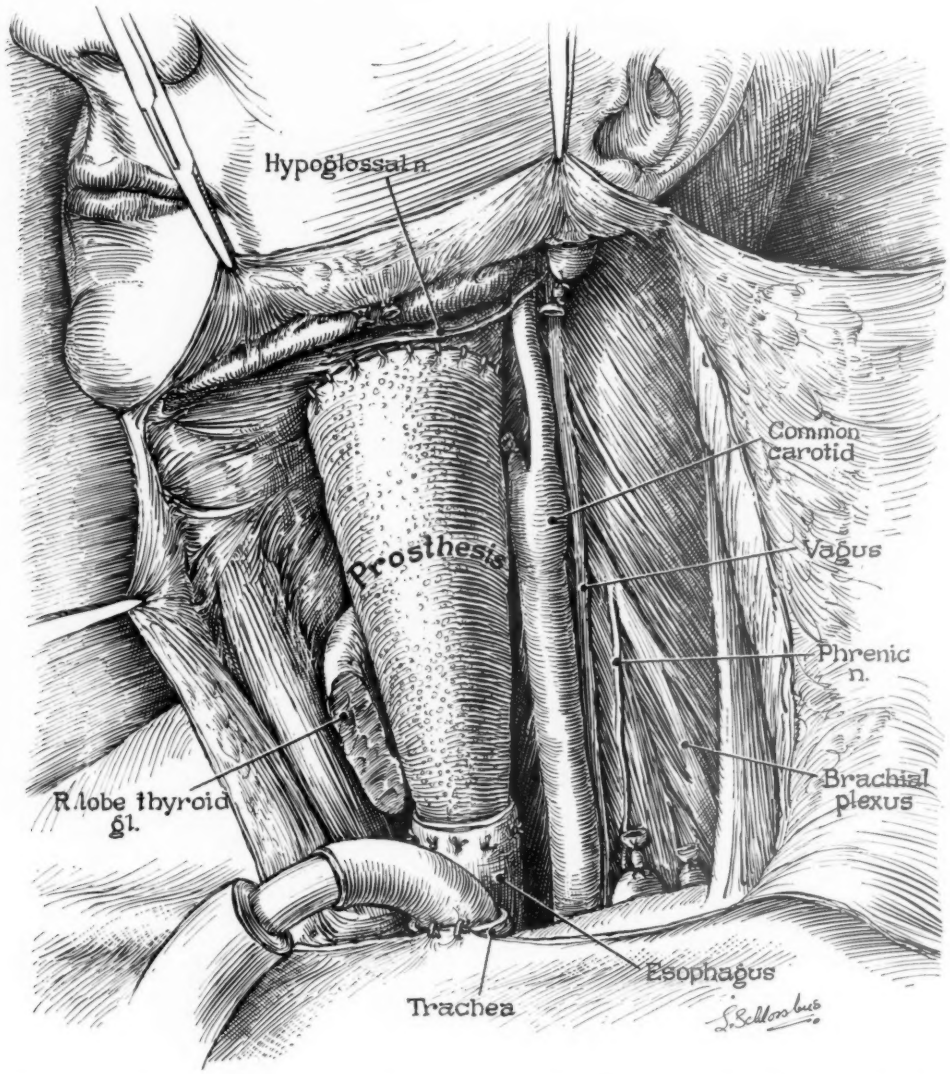


Fig. 3, *C*.—The prosthesis is now in position and it may be seen how the vascular nature of all the surrounding structures of the neck serve as a bed for the new graft. The prosthesis is fitted within the esophagus at the lower end to avoid possible fistula formation.

operatively and perhaps prevent late stricture, by offering immediate substitution for tracheal mucosa. Encouraged by the reconstructions of the esophagus, I had the opportunity to work* on another patient with a primary carcinoma of the trachea just above the carina. A tubular segment of treachea was resected and replaced by a tube of tantalum mesh covered by a split-thickness skin graft as described above, the only difference being that the epidermis was

*With Dr. Richard Kieffer, Jr., of the general surgical service.

removed from the skin graft with the hope that the transplant might be surgically more acceptable. The tantalum mesh overlapped the outside of the trachea in order to avoid any possibility of its becoming displaced within the lumen and causing respiratory obstruction. The patient withstood the procedure well and his stridor was relieved postoperatively. A bronchoscope was

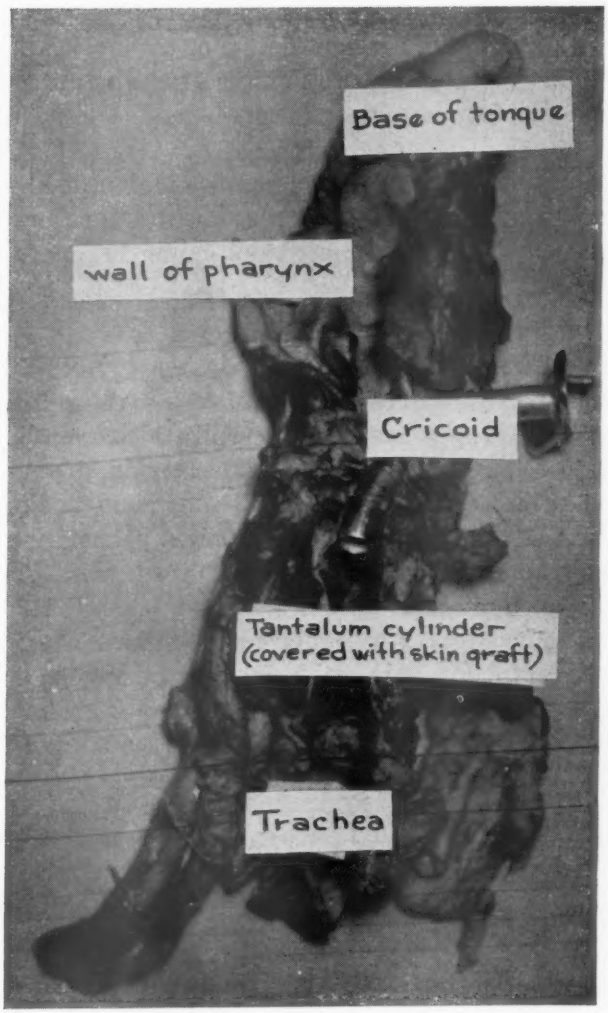


Fig. 4 (Case 5).—Specimen on the first patient in whom we replaced a segment of trachea using the same technique. A primary carcinoma of the trachea was removed just above the carina and the cylinder can be seen in good position over two weeks later. The patient did well until the fourteenth postoperative night at which time he suffered a sudden hemorrhage. We had not realized that the tracheotomy tube extended down into the reconstructed segment and the constant changing and cleaning of this tube may have had something to do with the postoperative hemorrhage.

inserted several times following operation and each time the tantalum mesh was clearly seen to have an adequate lumen. Fourteen days postoperatively when his wounds were healed and he was fully ambulant the patient had a sudden massive hemoptysis, aspirated blood, and died. Autopsy showed (Fig. 4) the tantalum mesh cylinder firmly in position with no evidence of any tendency

of the mesh to be taken up by the surrounding tissues. The hemorrhage had apparently occurred at the site of the ligated right vertebral artery. It had not been appreciated that the tracheotomy tube extended down into the reconstructed segment, and it is possible that trauma from this tube may have had something to do with the hemorrhage. Microscopic examination of the skin graft showed it to be taking nicely, and in contact with the surrounding mediastinum. Subsequently, Dr. Kieffer and Dr. J. C. Handelsman treated another patient with a primary carcinoma of the trachea, again using essentially the same technique. To this date, two months after the operation, that patient has done well, and the details of management of anesthesia and postoperative care are being reported in another paper.

The effect of this method of tracheal reconstruction on the patient's ability to cough up secretions if the reconstructed segment is long, may help to demonstrate whether or not continuous ciliated epithelium is essential to good function in the trachea.

SUMMARY

Early reconstruction of the cervical esophagus and pharynx is a prime requisite of any operative attack upon cancer of the oral cavity, pharynx, hypopharynx, or cervical esophagus. Free split-thickness skin grafts seem to serve adequately to replace the lining of esophageal and pharyngeal segments. These skin grafts have been applied by fastening them to the external surface of a metallic mesh. The mesh in such cases serves primarily as an elastic mold or stent, and may actually be removed later if desired. The cases of four patients in whom such reconstructions have been carried out are presented. Such patients not only swallow a regular diet without pharyngeal muscle but also develop an acceptable esophageal voice. The possible application of this technique to the reconstruction of tracheal defects is also discussed and mention is made of two cases in which such a method has been employed.

REFERENCES

1. Belsey, R.: Resection and Reconstruction of the Intrathoracic Trachea, Brit. J. Surg. **38**: 200, 1950.
2. Clagett, O. T., Grindlay, J. H., and Moersch, H. J.: Resection of the Trachea, Arch. Surg. **57**: 253, 1948.
3. Edgerton, M. T.: Replacement of Lining to the Oral Cavity Following Surgery, Cancer **4**: 110, 1951.
4. Handelsman, J. C., and Kieffer, R.: Resection of Thoracic Trachea for Carcinoma. In press.
5. Rob, C. G., and Bateman, G. H.: Reconstruction of the Trachea and Cervical Esophagus, Brit. J. Surg. **37**: 202-205, 1941.
6. Taffel, M.: The Repair of Tracheal and Bronchial Defects with Free Fascia Grafts, SURGERY **8**: 56, 1940.
7. Ward, G., and Robben, J. O.: A Composite Operation for Radical Neck Dissection and Removal of Cancer of the Mouth, Cancer **4**: 98, 1951.
8. Wookey, H.: The Surgical Treatment of Carcinoma of the Hypopharynx and the Oesophagus, Brit. J. Surg. **35**: 249, 1948.

ESOPHAGEAL DYSFUNCTION IN THE RAT AFTER VAGOTOMY

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THE innervation of the cardia and of the lower portion of the esophagus has been a subject of considerable interest both to clinicians and to experimental workers, and interest has been directed particularly toward the effects which follow vagal section. Numerous reports were found in which the effect of this procedure on the dog, the cat, and the rabbit was discussed, but only two publications were noted in which the rat was used as the experimental animal; of these only one, that by Houssay,[1] was concerned with the involvement of the cardia and the lower portion of the esophagus. In his animals, transabdominal vagotomy was found to result in esophageal dilatation, regurgitation of food, loss of weight, and death in many cases. In a series of complete gastrectomies in rats esophageal disturbance was not observed even though both vagus nerves had been severed. It therefore was deemed advisable to make further studies of the effect of bilateral vagotomy in the rat.

METHODS AND MATERIALS

Male albino rats which weighed 150 to 250 Gm. were used, and when possible litter mates were studied as a group. Daily records of weight and intake of food before and after operation were kept and observations were made of the animals' behavior. Roentgenologic studies were conducted as desired, the animals being fasted twenty-four hours without water for this purpose, then allowed to feed naturally from a barium-milk-sugar mixture. Esophageal activity was observed roentgenoscopically and, when necessary, films were exposed.

The following operations were conducted under ether or Nembutal (1 mg. per 40 Gm. body weight intraperitoneally) anesthesia:

Vagotomy.—Both vagus nerves were simultaneously sectioned between ligatures at the following points in their course along the esophagus: (a) at the esophagogastric junction, (b) at approximately the middle of the abdominal esophagus, (c) immediately distal to the diaphragm, (d) immediately above the diaphragm, and (e) at the point of emergence of the vagus nerves from the lung roots.

A two-stage operation was performed where the right vagus nerve was sectioned in the thorax immediately distal to the root of the lung, or immediately above the diaphragm, and later the left vagus nerve was transected in the midcervical region.

Combined Removal of Celiac and Superior Mesenteric Ganglia With Section of Right and Left Splanchnic Nerves.—The celiac and superior mesenteric ganglia were removed together with the bulk of the tissue lying in the area bounded by

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the abdominal aorta and the celiac and superior mesenteric arteries. At the same time the right and left splanchnic nerves were sectioned between their entrance into the abdomen and their union with the celiac ganglion.

Frequently this operation was combined with that of transabdominal vagotomy at the cardia, or was performed later after vagotomy.

Cardioplastic Operation.—Two types of operation were performed in an attempt to dilate the cardiac permanently: *Type A.* A longitudinal incision was made at the anterior esophagogastric junction down to but not including the mucosa, and the muscle fibers were pulled apart sufficiently to permit the mucosa to protrude. *Type B.* A longitudinal incision was made into the esophageal lumen 0.5 cm. from its termination and was continued through the cardia to extend a similar distance on the anterior wall of the stomach. The wound was then closed in transverse fashion with interruped sutures. In some instances transabdominal vagotomy at the cardia was combined with an operation of type A or B.

Complete Gastrectomy.—Total gastrectomy, in cases in which intestinal continuity was restored by end-to-end esophagoduodenal anastomosis, was performed in a number of animals. At times it was performed after transthoracic or transabdominal vagotomy. In a few instances partial gastrectomy, which involved removal of the rumen of the stomach, was carried out. Subsequently vagotomy was performed, or the vagal nerves were transected at the time gastrectomy was performed.

Dissections also were performed to follow the course of the vagus nerves in the neck and thorax and their distribution to the lower portion on the esophagus, cardia, and stomach. Necropsy was conducted on all dead or killed animals and appropriate histologic sections were obtained.

RESULTS

Transabdominal Vagotomy.—No essential difference was noted to result from variation in the point of vagal section within the abdomen. The results were classed in two main groups. In the first, twelve out of forty animals showed rapid progressive loss of weight, varying from 17 to 67 per cent of the preoperative level, till death occurred between the eleventh and sixteenth days. Difficulty in swallowing and regurgitation of gastric contents was observed, especially in the terminal stages; activity was subnormal and there was marked pallor of the eyes and ears.

In the second group composed of thirty-eight rats, rapid loss of weight was again a feature, but after fourteen to forty-two days gradual gains in weight were recorded and the preoperative level of weight was reached around the forty-second day in 50 per cent of the animals. Recovery was more delayed in the remaining members, though in all cases the preoperative levels were eventually passed.

Roentgenologic studies showed that transabdominal vagal section had a profound influence on the normal transport of material from the pharynx to

the stomach. The following points were shown to a greater or lesser degree by all animals examined, being more marked in those animals which died by the eleventh or sixteenth day.

Varying degrees of dilatation of the abdominal or thoracic portions of the esophagus or both were observed; there was regurgitation of material from the stomach or abdominal esophagus into the thoracic portion during feeding, and in all but two cases regurgitation continued for considerable periods after removal of the food. Retention of considerable amounts of barium in the thoracic or abdominal portions of the esophagus or both was noted both during and after feeding. The barium swallowed was seen to halt at the cardia for long or short periods, generally at the commencement of feeding but also during feeding in some instances. Filling of the stomach was delayed in about 40 per cent of the rats examined; in the remainder there was little variation from the normal.

The following features were seen in animals found dead or killed when moribund. The abdominal portion of the esophagus and especially the thoracic portion were dilated, and occasionally the cervical region also was involved. The esophageal walls were thin and flabby and the lumen filled with frothy mucus. Dilatation of the stomach especially of the rumen was noted, while the intestines were empty and often stained with bile. In no instance was any constriction apparent in the region of the cardia. Marked dehydration was constant. Evidence of inhalation of regurgitated material was found in a few instances.

Transthoracic Vagotomy.—Section of the right vagus nerve alone, either immediately above the diaphragm or just distal to the lung roots did not cause loss of weight or change in feeding habits. Simultaneous section of the vagus nerves immediately distal to the lung roots, or section of the right vagus nerve alone at this point with later section of the left vagus nerve in the midcervical region was followed in all cases by extremely rapid loss of weight, difficulty in swallowing, increasing weakness, regurgitation, and advanced dehydration. Death occurred between the seventh and fourteenth postoperative days. Section of the right vagus nerve immediately above the diaphragm, followed at a later date by section of the left vagus nerve in the midcervical region, generally resulted in death, although one rat survived. This rat subsequently was found to remain on a low weight level and only minimal weight gains were recorded. When the point of simultaneous vagal section was definitely located immediately above the diaphragm there was initial rapid loss of weight followed by indefinite survival at low weight levels accompanied by signs of inanition.

Section of the right vagus nerve alone was shown by roentgenologic studies to be without effect on esophageal activity. By similar means a marked dilatation of the abdominal esophagus and of the lower two-thirds of the thoracic portion was revealed in those animals with double vagotomy immediately above the diaphragm. Barium was retained in the thoracic portion up to thirty minutes after the cessation of feeding, accompanied by marked and frequent contraction of the thoracic esophageal wall. Considerable fluctuation of the column of retained barium synchronous with respiratory and abdominal movements also was noted.

Necropsy revealed marked dilatation of the entire esophagus and of the stomach, and an apparent constriction of the esophagus was noted at the diaphragmatic hiatus.

In the other rats in this group in which section of the nerves had been performed at high levels in one or two stages, complete paralysis of the cervical and thoracic esophageal region was observed on roentgenologic examination. The esophageal walls were flaccid and widely dilated, and no active movement of the esophagus was seen, the wide column of barium being slowly and irregularly driven toward the stomach by the addition of each swallowed mass. Retention at the diaphragm was a constant finding, and in one case it lasted for as long as twelve hours after food had been removed.

Considerable esophageal dilatation was found at necropsy, associated with apparent diaphragmatic constriction.

Combined Removal of Celiac and Superior Mesenteric Ganglia With Section of Right and Left Splanchnic Nerves.—After the procedure just described, evidence of difficulty in feeding or of regurgitation was not noted and abnormality of esophageal movement was not seen on roentgen-ray examination.

When transabdominal vagotomy was performed simultaneously with, or subsequent to, this type of sympathectomy, the results obtained were essentially similar to those which followed vagotomy alone. It was noted, however, that generally the stomach was filled on cessation of feeding and that there was little or no regurgitation after feeding.

Cardioplastic Operation.—No alteration in feeding behavior followed operations designed solely to dilate the cardia. When both vagus nerves were severed transabdominally, either at the time of the cardioplasty or at a later date, rapid loss of weight and regurgitation were observed, the symptoms being more severe than those noted after simple transabdominal vagotomy. At necropsy the stomach was dilated and distended with gas and the abdominal and thoracic portions of the esophagus were greatly dilated. In each case the cardia was shown to be widely patent.

Complete Gastrectomy.—Removal of the entire stomach was of necessity accompanied by simultaneous section of both vagus nerves at the cardia. In no instance was this followed by the esophageal disturbance characteristic of vagotomy performed at the level of the cardia, the stomach being left undisturbed. Complete gastrectomy also was performed on three rats in which the vagus nerves had previously been sectioned at the level of the cardia, and in which the stage of gradual increase of weight had been reached. Alteration of esophageal incoordination occasioned by vagotomy was not observed.

Partial gastrectomy was followed by slight regurgitation during feeding, but there was no esophageal dilatation or retention of barium; the esophagus became and remained completely empty after the last swallow of barium had entered the stomach. When transabdominal vagotomy was performed simultaneously with partial gastrectomy some regurgitation during feeding and slight retention of barium extending into the lower thoracic quarter of the esophagus resulted. Complete emptying, however, was found twelve minutes after the cessation of feeding.

DISCUSSION

In the normal rat the entrance of food into the esophagus was followed by a sequence of events whereby the food bolus was transported readily and without interruption into the stomach. Appreciable interference with this orderly progression was noted after vagal section, and variations occurred in relation to the point of nerve section.

When both vagus nerves were simultaneously sectioned at any point between the diaphragm and the cardia, the coordination between the esophagus and the cardia was completely interrupted, so that food arriving at the terminal portion of the esophagus was commonly held up at the cardia for varying periods. Nonetheless it was felt that cardiospasm, such as has been described in man and in some animals was not present as food entered the stomach during or shortly after feeding. In addition, when the cardia was rendered more patent and the vagus nerves were divided at this level, the subsequent course of events was more rapid and more disturbed than after vagotomy alone. It was thought that this temporary halting was due to mechanical factors, the crisscross arrangement of muscle fibers at the esophagogastric junction presenting an obstruction to food in the dilated abdominal portion of the esophagus. The retention of barium which was observed in the abdominal portion or the lower thoracic portion of the esophagus, or in both, and which was present for long periods after the cessation of feeding, also was thought to be mechanical in origin. At the diaphragm and at the cardia the diameter of the esophagus increased little, if any, so that at these points relative narrowing was present when compared with the diameters immediately above and below, and a virtual obstruction resulted.

Another feature of transabdominal vagotomy was that of regurgitation of barium, during and after feeding, from the stomach into the abdominal or thoracic portion of the esophagus. Zeller and Burget,[2] working with dogs, noted receptive relaxation of the cardia and stomach when the upper portion of the esophagus was distended, and found that this coordination was destroyed by vagal section in the neck. In this study in the rat, transabdominal vagotomy was followed by interruption of such coordination. Often the first barium swallowed was seen to enter the stomach directly, where it was retained for one to two seconds. It was then regurgitated suddenly into the abdominal or thoracic portion of the esophagus, or both. This regurgitation was not related to respiratory or abdominal movements and was commonly seen throughout the feeding period. In some instances it was more pronounced in the interval which followed removal of the barium meal and was noted to persist for as long as three hours. The expulsion of gastric contents into the abdominal or lower thoracic portion of the esophagus would frequently initiate a contraction wave which would travel in an antiperistaltic manner and would drive the barium to the level of the first rib or even to the pharynx.

Marked dilatation of the abdominal, thoracic, and sometimes cervical portions of the esophagus was present after transabdominal vagotomy, the greatest increase in diameter being in the lower thoracic portion. At necropsy the esophageal wall was seen to be thin, flaccid, and greatly dilated. It was felt

that this dilatation was the result of an atonic dilated stomach acting as a reservoir from which food material was regurgitated into the esophagus, and from the chaotic disordered esophageal movement, rather than from interruption of the nerve supply to the esophageal wall itself. Support for this opinion was afforded by the following points:

1. Dilatation or disorder of the esophagus was not seen to follow complete gastrectomy in which the vagal fibers were of necessity severed in the same position as in some types of vagotomies. Also, when partial gastrectomy was combined with vagotomy, comparatively little regurgitation and retention occurred. It was interesting to note that once the esophageal disturbance was established, neither complete nor partial gastrectomy produced any amelioration.

2. Atony and paralysis of the esophagus followed vagal section at points above the lung roots, but not when section was performed at lower levels. Regurgitation was not a feature in the group when vagotomy was performed at a high level. The complete esophageal paralysis was manifest in the manner in which the wide column of barium was driven slowly down the esophagus by the impact of each bolus of food, and by the animal's attempts to swallow during feeding.

3. In transabdominal vagotomies and in those instances in which section was definitely limited to the site immediately above the diaphragm, active and frequent contractions of the esophageal walls were observed, and regurgitation was present.

As a result of the interferences with the normal progression of food from the pharynx into the stomach, two main groups were noted. In one group the disturbance was sufficiently severe to prevent adequate intake of food, and the animals died from inanition, usually about the eleventh day after operation. In the other group intake of food was sufficiently reduced to cause an initial rapid loss of weight, but subsequently enough nourishment was obtained to maintain this low weight or to cause a gradual and sustained gain.

The series followed was too small to provide the basis for a definite opinion, and it was recognized that all of the sympathetic fibers to the stomach and cardia may not have been interrupted; however, the removal of the celiac and superior mesenteric ganglia combined with section of the splanchnic nerve was found not to alter the behavior of the animal. When this operation was performed prior to, or with, bilateral transabdominal vagotomy, it was shown that esophageal dilatation and regurgitation still occurred. This result was in contrast to the observations made on the cat by Knight,[3] but was similar to the findings in the dog by Zeller and Burget,[2] and in the same animal by Hwang, Essex, and Mann.[4]

SUMMARY AND CONCLUSION

In the rat, dilatation of the esophagus, especially the thoracic portion, regurgitation, and retention of food were noted to result from transabdominal vagal section, and from transthoracic section where the point of transection was located immediately above the diaphragm.

This interference with the normal progression of food down the esophagus resulted in the death of twelve of forty animals.

Operations designed to render the cardia more patent were found to increase the severity of the symptoms which followed vagal section.

The presence of some or all of the stomach was necessary for the development of the esophageal disorder, but once established, no alteration of the condition was produced by complete or partial gastrectomy.

Bilateral vagotomy at levels higher than a point immediately below the lung roots was shown to cause complete esophageal paralysis and death in all cases.

No alteration of the course which followed transabdominal vagotomy was occasioned by interruption of the sympathetic nerve supply to the stomach and cardia either prior to, or when combined with, section of the vagus nerves.

REFERENCES

1. Houssay, H. E. J.: Megaesófago por vagotomia infradiafragmática en la rata, Rev. Soc. argent. de biol. 23: 294-298, 1947.
2. Zeller, Werner, and Burget, G. E.: A Study of the Cardia, Am. J. Digest. Dis. 4: 113-120, 1937-1938.
3. Knight, G. C.: The Relation of the Extrinsic Nerves to the Functional Activity of the Oesophagcs, Brit. J. Surg. 22: 155-168, 1934.
4. Hwang, Kao, Essex, H. E., and Mann, F. C.: A Study of Certain Problems Resulting From Vagotomy in Dogs With Special Reference to Emesis, Am. J. Physiol. 149: 429-448, 1947.

THE EFFECT OF ACTH ON AUTOGENOUS AND HOMOLOGOUS SKIN GRAFTS IN RABBITS

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DURING the past two decades transfer of human skin from one individual to another has been extensively studied and documented. Excluding the transfer of skin from one identical twin to the other, it is presently accepted that these homologous grafts do not survive permanently. However, evidence of growth does persist for four to six weeks, following which the grafts invariably undergo degeneration. Medawar,[1-6] in a series of well-controlled rabbit experiments, has postulated that the antigen-antibody reaction with its resultant immune response accounts for the ultimate disappearance of the homologous skin in recipients. The reported effectiveness of ACTH in controlling the immune response[7] has suggested that homologous skin grafts might persist permanently or at least survive beyond the usual four- to six-week period if ACTH were given to inhibit this immune reaction. Whitelaw[8] has recently reported survival of homologous pinch grafts longer than sixty days in one burn patient treated with ACTH. It therefore becomes apparent that if homologous skin can be aided to survive for prolonged periods the treatment of severe burns will be greatly facilitated.

In conjunction with similar studies on human subjects, we have performed a series of homologous skin grafts in rabbits using ACTH in one group, and observing other grafted animals as controls. Free, full-thickness skin grafts were used despite increased difficulty in obtaining "takes," to prevent confusion with regard to healing by scar epithelium. If growth of full-thickness homologous skin could be obtained with ACTH therapy, split-thickness skin might be expected to survive more readily.

EXPERIMENT

Sixteen adult, well-nourished rabbits weighing 5 to 8 pounds were selected for the experiment. They were grouped in pairs, and sites for taking the grafts were selected on the back of each animal adjacent to the scapula bilaterally. Six rabbits were used for grafting and treatment with ACTH, while ten rabbits were to act as controls, receiving no hormone.

Intraperitoneal Nembutal anesthesia was employed and full-thickness skin measuring 3 cm. square was removed from the two areas outlined on the back of each animal. Transfer of the grafts was accomplished according to the diagram in Fig. 1. The skin from the left side of each animal was transferred to the right side of the same animal so that each rabbit might act as his own

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control. The skin from the right side of each animal was in turn transferred to the left side of the companion rabbit to act as the homologous graft. Bolster-type dressings of lambs' wool were applied and sealed with collodion. The hind legs were hobbled in plaster of Paris to prevent the animals from disturbing the operative field. Following the initial portion of the experiment, hobbling was found to be insufficient for protection of the grafts. Control animals had to be repeated using thin plaster of Paris jackets over the grafts.

The ACTH was administered in a dosage of 4 mg. per kilogram per day, given in equal doses at eight-hour intervals. The therapy was started twenty-four hours prior to operation and continued for twenty-two days. The response to the hormone was measured by daily eosinophile counts for three days, and subsequently, every three days for twenty-two days. An adequate therapeutic response was obtained in all the animals. Biopsies were taken of all the grafted areas at the completion of the experiment.

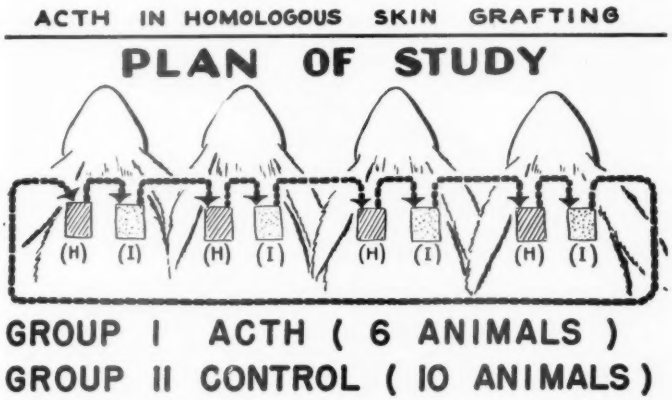


Fig. 1.—Diagram showing the method of transfer of skin. Grafts from the left side of each animal were transferred to the right side of the same animal, while the graft from the right side was transferred to the left side of the companion rabbit.

Previous reports have shown maximal viability of homologous split-thickness skin grafts in rabbits to be about ten days. Accordingly, dressings were removed and grafts inspected on the tenth postoperative day in this experiment. At this time the autogenous grafts were observed to be growing in all subjects receiving ACTH, as evidenced by apposition of skin edges, growth of hair, and texture of the graft. By contrast, the homologous grafts had already become hardened, contracted, and discolored, with separation of skin edges indicating little, if any, possibility of eventual survival (Fig. 2, *A*). Evidence of scar epithelium growing beneath these grafts was obvious by the fourteenth postoperative day.

Degenerative changes in the homografts continued steadily, along with concomitant scar epithelization beneath the contracted edges from the periphery, until the homologous grafts had disappeared completely, as shown in the photograph taken on the twenty-sixth postoperative day (Figs. 2, *C* and 3, *B*). On the other hand, the autogenous grafts showed that healing had taken place at the margins of the grafts, and in some the hair was growing in the opposite

A.

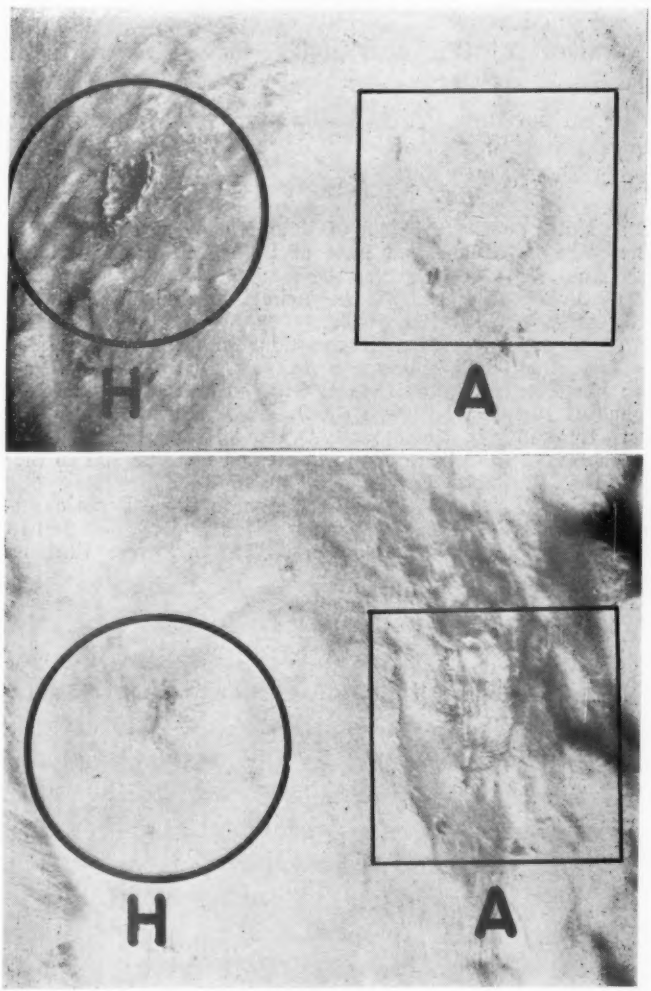
B.

C.

Fig. 2.—Photograph of the grafted areas at A, ten days, B, eighteen days, and C, twenty-six days. Note the difference in color, contraction, and separation of skin edges as early as the tenth day in the homologous grafts.

direction where the transplants were inadvertently turned around (Fig. 3, *B*). Biopsies of these transplants disclosed a microscopic picture of the usual fibrosis and scarring.

A.



B.

Fig. 3.—Photograph showing grafted areas at eighteen days and twenty-six days. The homologous graft is ready to slough while the autogenous graft is growing. Note the hair growing in the opposite direction in *B*, where the autogenous graft was inadvertently turned around. *A*, Series A, No. 11, eighteen days. *B*, Series A, No. 11, twenty-six days.

In the control group of animals none of the homologous grafts were viable on the tenth postoperative day, and of the autogenous grafts, only 60 per cent survival was obtained. This decrease in "takes" of autogenous grafts of the control group could be explained by the extent to which the animals disturbed the operative field. This impression was borne out by the animals that were placed in plaster of Paris jackets, where 100 per cent "takes" of autogenous grafts were obtained.

It becomes apparent from the above described experiment that little benefit can be expected from ACTH as an adjunct in aiding the survival of homologous

full-thickness skin grafts in rabbits. Likewise, we have gained the impression that the healing and survival of autogenous full-thickness grafts have not been greatly influenced by ACTH therapy.

CONCLUSIONS

1. The survival of full-thickness homologous skin grafts in rabbits is not prolonged by the use of ACTH.

2. Healing of autogenous grafts takes place at a normal rate despite treatment with ACTH.

REFERENCES

1. Medawar, P. B.: Notes on the Problem of Skin Homografts, Bull. War Med. 4: 1, 1943.
2. Medawar, P. B.: The Behaviour and Fate of Skin Autografts and Skin Homografts in Rabbits, J. Anat. **78:** 176-199, 1944.
3. Medawar, P. B.: A Second Study of the Behaviour and Fate of Skin Homografts in Rabbits, J. Anat. **79:** 157-176, 1945.
4. Medawar, P. B.: Immunity of Homologous Grafted Skin; Suppression of Cell Division in Grafts Transplanted to Immunized Animals, Brit. J. Exper. Path. **27:** 9-15, 1946.
5. Medawar, P. B.: Immunity in Homologous Grafted Skin. II. The Relationship Between the Antigens of Blood and Skin, Brit. J. Exper. Path. **27:** 15-24, 1946.
6. Medawar, P. B.: Immunity in Homologous Grafted Skin. III. The Fate of Skin Homografts Transplanted to the Brain, to Subcutanous Tissue and to the Anterior Chamber of the Eye, Brit. J. Exper. Path. **29:** 58-69, 1948.
7. Harris, S., and Harris, T. N.: Effect of Cortisone on Some Reactions of Hypersensitivity in Laboratory Animals, Proc. Soc. Exper. Biol. & Med. **74:** 186-189, 1950.
8. Whitelaw, M. J.: Physiological Reaction to ACTH in Severe Burns, J. A. M. A. **145:** 85-89, 1951.

THE USE OF THE THERAPEUTIC "WATER BED" IN SURGICAL LESIONS

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THE concept of treating disease by immersion is not new. As early as 1832 both Neal Arnoth in England and Beaupre in France had treated decubitus ulcers by prolonged baths. In 1855, when von Langenbeck recommended the "water bed" for the treatment of large wounds, he stated that patients could be kept in water for long periods of time, from days to months.

The prolonged bath therapy was first introduced in Austria by Ferdinand von Hebra in 1861, and was recommended as an important adjunct to therapy. In 1877 Hans von Hebra reported the beneficial effects of this therapy in surgical lesions (gangrene of the skin and subcutaneous tissues), as well as in dermatological lesions (burns, psoriasis, pemphigus, etc.).

The significance of continuous water bed therapy for the treatment of surgical lesions was really appreciated in Vienna during World War I. At the beginning of the war, Riehl reported the striking effects of this form of therapy on gangrene, phlegmon, and severe ulcerative processes, and stated that he had never seen a wound infection develop under water bed therapy. The method received a full scale test after 1917, when Eiselberg and Riehl succeeded in setting up a water bed ward of approximately twenty beds in the Allgemeines Krankenhaus. Reports from Eiselberg and von Sacken covered a number of diseases to which this therapy was applicable, together with the advantages and drawbacks of the method. Other authors, in particular B. Pfab of the Klinik Eiselberg, studied its application to civilian surgery and investigated its modus operandi as well as the effect of the therapy upon the individual as a whole.

As the basis for prolonged bath therapy has become firmly established, the interest in this form of treatment has steadily increased. Water bed installations were organized in almost all large hospitals in Vienna and in many provincial hospitals as well. In this way a large proportion of Austrian physicians have come to appreciate the advantages of this form of therapy, and today it is considered one of the most important methods of treatment. Because of this background, we have been very interested to learn from foreign visitors that the method is almost unknown elsewhere, and that this therapeutic modality was first seen by them in our hospitals.

In the following paragraphs I wish to indicate briefly the indications for water bed therapy in surgery on the basis of our own experiences. Its use in other specialties—dermatology, gynecology, etc.—will not be discussed because of space limitation.

The construction of a water bed has gone through many changes from the primitive form to the modern. The bed described by Hebra was made of wood,

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while the modern bed is made entirely of metal. Some of the tubs have double walls to prevent rapid cooling of the warm water. The tub is filled with water at 30° C., as this temperature is most agreeable to the average patient. The desires of occasional patients for slightly higher temperatures should be fulfilled. At the head end of the tub there are the usual fixtures to provide for a mixture of hot and cold water. The temperature may be controlled manually or by thermostat. At the foot end there are two outlets, as well as an emergency outlet to prevent overflow.

The water is changed daily, at which time the entire device is cleaned. In the tub there is a metal spring bed frame with adjustable head and foot pieces, mattress, pillow and bed linen upon which the patient lies. This bed frame is best equipped with a hoist arrangement so that it may be lifted in and out of the water at will.

From the surgical viewpoint, water bed therapy should be considered, and is recommended, for the following:

1. Decubitus Ulcers.—The fresh, progressing bed sore comes to a standstill in a few days because, due to buoyancy, the involved tissues are no longer subjected to pressure and may recover. Necrotic tissue demarcates and sloughs rapidly, and as there is no pressure obstacle to vascularization, rapid growth of epithelium is secured. Old, neglected, and extensive bed sores which have resisted treatment in the conventional bed can be checked and eventually healed. This is, of course, in the event that the individual resistance and ability to regenerate tissue has not been unduly depressed. In particular, the paraplegic patients whose decubitus ulcers appear shortly after acquired injury belong in this group. Abundant evidence of the value of this therapy was seen in wartime. If the diagnosis of complete cord severance can be made, there is no place for laminectomy, but if the decubitus ulcers can be healed in the water bed, these patients are freed from the risk of ascending infection (pyelonephritis) and its consequences (amyloidosis). Many of these patients can be made ambulatory with braces. I have seen a number of these patients who have become self-supporting.

Even for those hopeless patients with evidence of urinary sepsis, the water bed is of inestimable value, as it permits them to spend their last days in comfort, free from the torture of frequent dressing change.

2. Phlegmon.—Severe phlegmons of soft tissue, particularly of the buttocks and upper thigh, are benefited, as the tissues are no longer injured by the weight of the body, and the patient is free from the frequently painful change of dressings, unavoidable in the dry bed.

Patients with dangerous pelvic phlegmon, as well as those with parasacral infection following sacrorectal resections, are also grateful subjects for this therapy. The therapy holds equal advantages for abdominal wall infections following operation for suppurative peritonitis (perforated appendicitis, perforated duodenal or gastric ulcer, gangrenous cholecystitis), and for operations for strangulated hernia with infection of the hernial sac and gangrene of the bowel.

It goes without saying that all wound interstices must be widely open before the patient is placed in the water bed. The wound must be opened sufficiently wide to provide easy access to the water. Profuse wound secretion decreases rapidly after but a few days, and necrotic tissue falls off and is replaced by granulation tissue.

Open amputation wounds, when infection is feared because of pre-existing gangrene or suppuration, show a tendency toward rapid healing. As long as there is no bare bone visible, slough of dead tissue occurs and epithelization begins, and in most cases skin grafting or plastic surgery is not necessary.

3. Postradiation Ulcer.—The water bed has a favorable influence on the poor healing of the postradiation ulcer (von Sacken, Kummer). After two or three months of treatment, these defects stabilize and begin to epithelize, although no previous therapeutic modalities have been of any aid.

4. Closure of Fistulas.—The water bed is one of the most certain methods to obtain spontaneous closure of various fistulas. Among these are biliary fistulas (postcholecystectomy without operative injury to the ductal system or after cholecystostomy), fistulas with pancreatic secretions (after extensive stomach resection for ulcer or carcinoma of the stomach), duodenal fistulas (after resection for distal ulcers or after exclusion resection with stump blowout), fecal fistulas (after injury, ileostomy for ileus, gangrene or phlegmon of the bowel, suture dehiscence, lateral colostomy), and urinary fistulas (after injury, cystostomy after prostatectomy).

The effect of continuous irrigation and the disposal of water waste products protects the surrounding skin from eczema and maceration, and, in consequence, spontaneous closure of the fistula obviates further surgery.

Lipped fistulas will require operative closure, since their nature makes spontaneous cure impossible. Even in these cases, the water bed is of great value in the care and preparation of the surrounding skin, and radical closure is thereby facilitated.

5. Fractures With Phlegmon Complications.—Compound fractures complicated by soft tissue phlegmon, and gunshot fractures threatened by gas phlegmon, are frequently aided by water bed therapy, whereas, with the conventional therapy, amputation is a frequent consequence. Water bed therapy does not contraindicate skeletal traction through the calcaneus. The fractured lower extremity, for example, is placed on a Braun's frame with skeletal traction, and the entire apparatus placed in the water bed. Abscesses and soft tissue pockets must be widely incised beforehand.

The favorable constitutional effects of water bed therapy, as well as its influence upon wound healing, may be explained by the following results of this therapy:

1. During therapy the leucocyte count is increased by one-third, with a decrease in the lymphocytes and increase in myelocytes.

2. During the stay in the water bed, blood pressure falls from 20 to 30 mm. of mercury. The most marked depression occurs after the third or fourth day. Pressure returns to normal within three to four hours after the patient

is removed from the water. The blood pressure drop is due to the heating effects of the surrounding water, and to complete muscular relaxation. This blood pressure drop also explains the unfavorable influence of this therapy upon cardiac lesions.

3. Prolonged water bed therapy produces an increased flow of wound secretion. The centripetal exudation also prevents deposition of bacteria from the water into the wound, and subsequently into adjacent tissue.

4. The inhibition of pathogens from stool and urine is caused by the oligodynamic action of the heavy metals with which the tub is lined. Copper, lead, and zinc are the most potent of the metals.

B. Pfab has shown that the activity of the oligodynamic substances is greater upon pathogens than nonpathogens. (P. Saxl states that the oligodynamic activity is physical, as the amount of metal which dissolves in the water is so small as to be demonstrable with difficulty, or present in such minute quantities that chemical activity is highly improbable.)

The removal of bacteria by the continuous flow of water combined with the oligodynamic activity necessarily influences suppurative processes. Furthermore, the bactericidal effect on pathogens and the increased exudation must play large roles in the healing process.

5. The diminished energy consumption and caloric needs while in the bath cause greater deposition of food elements and an increase in weight, which explained to some extent the improvement in over-all status.

CONTRAINDICATIONS

Patients with circulatory disturbances, heart failure and myocardial degeneration, as well as those with pneumonia or bronchitis, tolerate water bed therapy very poorly. Thorough study of the cardiac and pulmonary status is highly advisable.

Patients with open empyema represent absolute contraindications.

ACCIDENTS DURING THERAPY

Nursing personnel must be constantly alert to prevent scalding of patients. They alone handle the intake valves as patients are inclined to increase unduly the heat of the water. With modern installations, an alarm system is available to prevent damage due to overwarm water.

The danger of drowning is prevented by the placement of rolled sheets under the axillas. The sheets are fastened to the bed which is upright in back, so that the patient cannot slip down. The patient must be prevented from drinking the water and from getting water in the ears to avoid pneumonia and otitis.

If bronchitis, pneumonia, or heart failure become apparent, the patient must be shifted to a dry bed immediately.

Blood coagulation on the wound surfaces is decreased in comparison to dry therapy. Consequently, the risk of late hemorrhage is increased, and particular

attention must be given to wounds with drainage, large raw surfaces (open amputation stumps), and small wounds from skeletal traction if secondary hemorrhage is to have timely treatment.

Aside from these dangers, many patients have unpleasant sensations in the first few hours of water bath therapy, which later disappear. Cachectic and markedly anemic patients complain of headache and excessive perspiration the first twelve to eighteen hours, during which time the face becomes alternately flushed and pale. This so-called "wasserbett kater" ("kater" resembles a "hangover") goes away after a few hours and, at the worst, after the first day. During the first two or three nights some patients complain of insomnia, which is also transient. In most cases annoying discomforts in the palms and soles develop due to softening of the skin, usually at about the third day. The discomfort lasts about two to three days and ceases when the thickened skin is cast off. Repeated applications of castor oil to the soles and palms help alleviate the discomfort.

The application of tar is useful therapy against the water bed eczema and water bed mycosis which begin with mild itching. A day of dry treatment causes these skin lesions to disappear.

In these few lines I cannot fully demonstrate the already proved therapeutic aid that continuous water bed therapy offers to medicine in general. Because this method is still little known and appreciated in other countries, I have discussed the method only enough to show the surgeon that in many cases water bed therapy can aid his patient, even to the extent of making the terminal stages of certain diseases more comfortable.

BIOLOGICAL PROPERTIES OF STARCH SPONGE AND STARCH SPONGE POWDER

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THE ideal sponge for internal application must be readily absorbed and produce no allergic or local tissue reactions, and should aid hemostasis. The potentialities of starch sponge were investigated by Bice, McMasters, and Hilbert[1] who first suggested its use in surgery in 1944. The simple method of production (freezing, thawing, and drying a 5 to 10 per cent starch paste), ease of sterilization, low cost, and long storage life have been factors which recently have aroused military interest in the sponge.

Objective studies on the physiologic properties of the starch sponge reported in the literature are limited. Correll, Prentice, and Wise,[2] in 1945, investigating chiefly the gelatin sponge, included results concerning starch sponge implants in rat muscle. It was not until 1949, however, that any extensive clinical or experimental investigations were reported by Rosenfeld.[3] The experimental work was on rabbits and was concerned for the most part with hemostasis, but the results of leaving large pieces of starch in the peritoneal cavity were also included.

The present study was designed to investigate (a) the physiologic absorption of the starch sponge, (b) local tissue reactions to sponge implants, and (c) its hemostatic properties.

SERIES I: ABSORPTION STUDIES

Methods.—Five mongrel dogs weighing 10 to 19 kilograms were anesthetized by an intravenous injection of 20 mg. of sodium pentobarbital per kilogram of body weight. Sterile surgical procedure was employed throughout. A dry, sterile starch sponge† was inserted between the loops of the intestine through a midline incision into the peritoneal cavity. The peritoneum was closed with sutures and another sponge of approximately the same size and weight implanted subcutaneously. A control animal was subjected to the same operative procedure but received no implant. Three of the animals were sacrificed at intervals of 6, 24, and 48 hours. At autopsy the free peritoneal fluid and the subcutaneous fluid were removed, centrifuged at 1,500 r.p.m. for 15 minutes, suspended in water and tested for starch with I_2-KI reagent. The supernate was tested for sugar with Benedict's qualitative reagent. Since the blood and tissue fluids normally contain sugar in low concentrations, trace reactions for sugar were recorded as negative. From the 3 remaining animals

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subcutaneous fluid at the site of implantation was aspirated and similarly tested at the end of 72 and 96 hours. These animals were spared for extended observation of local effects, healing, and adhesions, the results of which are included more appropriately with the animals of Series II.

Results.—One-half hour after implantation, palpation of the subcutaneous implant revealed that the edges had become rounded and the surfaces soft. A firm mass was still present after an hour but the sponge was impalpable two hours after implantation. At the time of autopsy (6, 24, and 72 hours) 10 to 12 ml. of sanguineous, viscous, subcutaneous exudate was recovered from each animal. When centrifuged, 50 per cent sedimentation resulted. The subcutaneous fluid aspirated from the 3 surviving animals at 96 hours was much less viscous and contained less than 2 per cent sediment. Serosanguineous peritoneal fluid, 90, 40, and 20 ml., was recovered from the 6, 24, and 72 hour animals respectively. The peritoneal fluid from the 6 hour animal contained approximately 5 per cent sediment by volume; the fluid from the 24 and 72 hour animals less than 0.5 per cent by volume.

From these data it is apparent that (a) the hydrolysis of starch into sugar occurs more rapidly in the peritoneal cavity than in the subcutaneous tissues, indicated by the early presence of sugar in the peritoneal fluid; (b) the absorption of the sponge from the peritoneal cavity is complete within 24 hours, demonstrated by a negative test for sugar at this time; and (c) the hydrolysis and absorption of the subcutaneous implant is accomplished within 72 hours, indicated by negative starch and sugar tests on the subcutaneous exudate.

SERIES II: LOCAL EFFECTS

This series was designed to determine whether increased inflammation or excessive adhesions occur in the presence of starch sponge, and to determine the effect of starch sponge on wound healing and the formation of scar tissue. Since starch sponge powder (ground starch sponge) has possible applications as a hemostatic on bleeding surfaces, this form of the substance was also studied.

Methods.—Five mongrel dogs were anesthetized as previously described. Bilateral symmetrical incisions approximately 5 cm. in length were made through the skin over the scapular area. Into one was sprinkled 0.25 Gm. of ground starch sponge; the other incision served as a control. Both wounds were closed with 0 braided silk suture and dressed with a dry gauze bandage. No local medication was used, but each animal received 300,000 units of procaine penicillin in peanut oil with aluminum monostearate intramuscularly one hour prior to surgery. The wounds were observed for inflammation and the progress of healing 3 times daily up to the fifth day. On the fifth day the skin sutures were removed and the wounds observed daily thereafter. The animals were sacrificed 30 days after the implants were made, and the treated and control wound areas were excised and fixed in 10 per cent formalin. Frozen sections were prepared and stained with Lugol's iodine. The surviving animals from Series I were similarly observed for a period of 30 days and then sacrificed.

Results.—In all 5 cases in Series II, minor local edema occurred in both the experimental and control wounds. The swelling attained its maximum size

on or about the second day. The edema gradually decreased and disappeared by the ninth day. No difference in healing between the control and the experimental wounds was apparent and after 30 days the scars could not be differentiated by gross inspection. Sections through the healed incisions were negative for starch particles.

Careful examination of the peritoneal cavities of the 3 animals reserved from Series I showed no evidence of adhesions 30 days after the implant. Grossly, the sites where the subcutaneous implants had been made revealed no excessive scar tissue. Microscopic examination of sections through the implanted area were negative for starch particles.

SERIES III: HEMOSTATIC QUALITIES

Hemostasis is aided by a material which mechanically retards or stops the flow of blood until the normal clotting mechanism occurs, or by a material which accelerates the clotting mechanism. This study was designed to determine the effects of starch powder on coagulation and to demonstrate the mechanical action of the sponge on hemostasis.

Methods.—The coagulation time studies were made in vivo by the following technique: The temporal muscles of a dog were exposed and the loose fascia removed. A highly vascular field composed of small vessels overlies the muscle in this area. A small vessel (arteriole) approximately 0.1 mm. in diameter was severed and the first few drops of blood were removed with a gauze sponge. An electric timer controlled by a foot switch was started as the next drop formed and a clean glass rod (diameter 0.5 to 1.0 mm.) was repeatedly drawn through the drop. As soon as the first fibrin strand adhered to the rod the time was recorded. The field was sponged dry and three drops allowed to form from the same bleeder. The field was sponged again and the procedure repeated with a clean glass rod, the tip of which carried by adhesion the substance to be tested. Clotting times were thus determined in the presence of starch and thrombin.* Thirty alternate starch-control-thrombin determinations were made on each of 5 bleeders, for a total of 150 tests in this group. This method was used in place of an in vitro technique to obtain relative times more indicative of the events actually occurring at a bleeding surface. Normal blood, and blood in the presence of starch, clot more slowly in vitro than in vivo, whereas blood in the presence of excess thrombin clots almost instantaneously both in vivo and in vitro; thus the relative clotting times determined by routine in vitro methods would be misleading.

Observations on the mechanical effect of starch sponge on hemostasis were made by the following method: The external jugular vein of a dog was exposed and punctured with an 18 gauge needle. A weighed starch sponge was placed over the puncture and maintained with just sufficient pressure to assure good contact but not to collapse the vein. After one minute the sponge was removed and reweighed. Since there was no leakage between the sponge and vessel, the

*Thrombin, Topical (Bovine Origin) Parke, Davis & Co., Detroit, Mich.

gain in weight was taken as the amount of blood lost before hemostasis occurred. This procedure was repeated with an ordinary gauze sponge. Five similar determinations were made.

To ascertain that the results were not a measure of the absorptive efficiency of the sponges, the animal was heparinized and the procedure described above repeated.

Results.—The clotting time studies show that by this method no statistically significant difference exists between the mean clotting time of normal blood and that of blood in the presence of starch. The mean clotting times obtained were 11.9 ± 2.1 seconds for untreated blood, 10.7 ± 2.0 seconds for blood to which starch had been added, and 3.6 ± 1.0 seconds for blood to which thrombin had been added. The clotting time difference between the untreated and thrombin-treated blood is highly significant.

TABLE I. SUMMARY OF THE RESULTS OF THE ABSORPTION STUDIES

DOG NO.	WEIGHT OF SPONGE (IN GRAMS)*		TIME AFTER IMPLANT (IN HOURS)	STARCH		SUGAR		ML. FLUID RECOVERED	
	IP	SC		IP	SC	IP	SC	IP	SC
1	4.0	4.0	6	+	+	+	–	90	12
2	4.0	3.5	24	–	–	–	+	40	10
3	3.7	3.9	48	–	–	–	+	20	12
4	3.5	3.6	72		–		+		
			96		–	–	–		
5	3.8	4.0	72		–		+		
			96		–		+		
6	3.7	3.5	72		–		–		
			96		–		–		

*Density approximately 0.13.
IP = Intraperitoneal.
SC = Subcutaneous.

The study comparing the effectiveness of the gauze and starch sponges in the control of normal bleeding from a punctate wound shows that with the starch sponge less loss of blood occurs. The average gain in weight for 5 tests with the starch sponge was 0.22 ± 0.02 Gm. as compared with 0.40 ± 0.07 Gm. for the gauze sponge. After heparinization, however, the gain in weight was approximately the same (0.81 ± 0.08 Gm. for the starch and 0.74 ± 0.04 Gm. for the gauze sponges) indicating that under these conditions both sponges are equally effective as absorbents.

Discussion.—These studies have shown that the absorption of the sponge is accomplished very rapidly, but is accompanied by an acute accumulation of serous fluid. These experiments do not demonstrate whether this is a specific tissue reaction to the starch or a nonspecific foreign-body reaction. However, the initial reaction does not appear to interfere with wound healing or to promote excessive scar tissue or adhesions. In this study it was not possible to demonstrate the presence of starch 30 days after the implant. However, Correll, Prentice, and Wise[2, 4] implanted thrombin impregnated pledgets of starch sponge in the femoral muscle of the rat and found fragments through the fiftieth day.

The presence of starch material does not significantly accelerate the clotting mechanism. Its hemostatic action therefore appears to be due to a mechanical action. The sponge, when applied to a bleeding area, softens, and conforms to the contours of the surface, and rapidly absorbs the free blood. When exposed to the large surface area in the sponge capillaries, the blood promptly clots. This area of the sponge is now incapable of absorbing blood and prevents the further loss of blood by mechanically damming the flow.

REFERENCES

1. Bice, C. W., McMasters, M. M., and Hilbert, G. E.: Proposed Use of Starch Sponges as Internal Surgical Dressings Absorbable by the Body, Science **100**: 227-228, 1944.
2. Correll, J. T., Prentice, H. B., and Wise, E. C.: Biologic Investigations of a New Absorbable Sponge, Surg., Gynec. & Obst. **81**: 585-589, 1945.
3. Rosenfeld, S. S.: Starch Sponge—A Hemostatic Agent, SURGERY **26**: 842-846, 1949.
4. Correll, J. T., and Wise, E. C.: Certain Properties of a New Physiologically Absorbable Sponge, Proc. Soc. Exper. Biol. & Med. **58**: 233-235, 1945.

Case Reports

PERIPHERAL BONE METASTASIS FROM CARCINOMA OF THE RECTUM

Review of the Literature and Report of an Unusual Case

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METASTASIS to bone from carcinoma of the rectum is generally considered to be a rare occurrence. Reports of such metastases have appeared in the literature from time to time, and the percentage of incidence has varied from 0.5 per cent to 10.5 per cent. It is difficult to arrive at a valid estimate of actual incidence, since some of the reports are based on a small series of carefully studied autopsy cases, while other estimates are based on larger case record series, in which the lesion was discovered by x-ray or actual biopsy. Aufses, in 1930, was able to find only sixteen reported cases of metastasis to bone from carcinoma of the rectum in a careful search of the literature back to 1870. To these he added an additional eight cases from his own study. It must be remembered, however, that inasmuch as x-ray survey of the skeleton was not commonly done prior to 1930, such metastases probably often went unnoticed. Since Aufses's report several notable additions to the subject have been made, and bone metastasis in carcinoma of the rectum is no longer acknowledged to be the rarity it was twenty-five years ago.

Nevertheless, metastasis to the peripheral long bones from carcinoma of the rectum is still a distinct rarity. Weston's review of the literature in 1942 revealed only five reported cases of metastasis to the humerus. Earlier, Bacon in studying a series of 366 cases of carcinoma of the rectum found two instances of metastasis to the femur. Abrams has reported a case with metastasis to the fibula, and Johnson and Janes reported a most unusual occurrence of metastasis to the talus in a patient with generalized metastases from carcinoma of the rectum. Decker and Fash very recently added a case with metastasis to the tibia.

Although the primary purpose of this report is to present an unusual case of metastasis from carcinoma of the rectum, the accompanying table is added to show more clearly the background of earlier studies and the relative distribution of reported metastases. The authors were unable to find any reported incidence of metastasis to the foot, other than the previously noted metastasis to the talus.

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TABLE I. REPORTED CASES OF METASTASIS TO BONE FROM CARCINOMA OF THE RECTUM, SHOWING DISTRIBUTION AND RELATIVE INCIDENCE

AUTHOR	TOTAL CASES OF CARCINOMA OF RECTUM STUDIED	TOTAL CASES WITH METASTASIS TO BONE	DISTRIBUTION AND RELATIVE INCIDENCE OF METASTASES															
			VERTEBRAE	SACRUM	RIBS	PELVIS	SKULL	STERNUM	SCAPULA	FEMUR	HUMERUS	RADIUS	ULNA	TIBIA	FIBULA	TALUS	METATARSAL
Aufses' review	196+	16	6	1	3			2	1	3	1	1	1				
Aufses	117	8	2	2	3	2	3	1		3	2						
Brown and Warren	170	13	10	5	2						1						
Geschickter and Maseritz	370	1									1						
Ghormley and Valls	3,800	19	6		1	8			1		3	cases to long bones					
Muller (Quoted by Ghormley and Valls)	57	6	Sites of metastases not mentioned														
Bacon	366	15	6		2		2	1	1	2							
Stein	270	16	Sites of metastases not mentioned														
Weston	1	1									1						
Johnson and Janes	1	1														1	
Decker and Fash	1	1												1			
Abrams	87	11	*		*	*	*		*					*	*		
Beskin and Atwood	1	1															1

*Number of metastases not mentioned by author.

The following case is remarkable in that it represents a solitary bony metastasis to the left fourth metatarsus, it being the only demonstrable metastasis in clinically a well patient six months after abdominoperineal resection for carcinoma of the rectum.

CASE REPORT

H. T. (No. 98125, 101494), a well-developed, well-nourished, unmarried 52-year-old white woman, entered the Truesdale Hospital for the first time July 4, 1950, with a chief complaint of rectal bleeding of four months' duration. She had enjoyed excellent health until about four months prior to admission at which time she began to note a small amount of bright red blood with each bowel movement. There had been no associated abdominal pain, change in bowel habits, or weight loss. System review and past history were both negative. Proctosigmoidos-

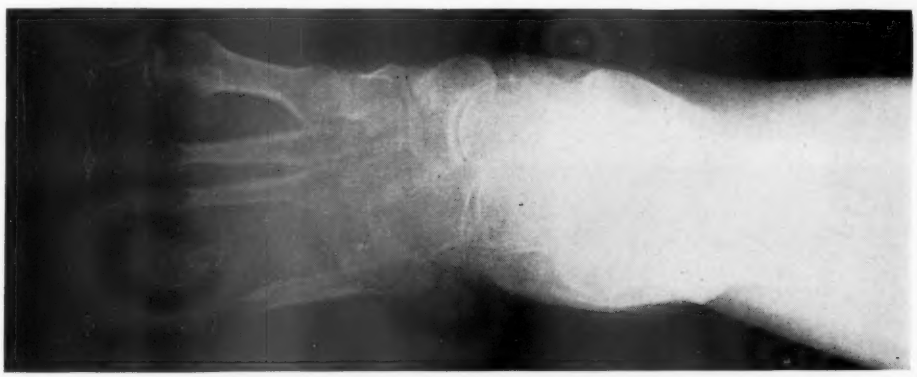

Fig. 1.—Anteroposterior roentgenogram of left foot showing almost complete destruction of fourth metatarsal by metastatic tumor.

copy performed prior to admission revealed a polypoid, fungating lesion in the rectosigmoid, biopsy of which disclosed adenocarcinoma. A barium enema done in the outpatient department showed a filling defect in the rectosigmoid consistent with a neoplastic lesion.

Physical examination on admission revealed the abdomen to be soft, with no palpable masses and no evident liver enlargement. Rectal examination could not digitally delineate the previously observed and biopsied rectal mass.

July 7, 1950, at operation, an annular, polypoid, fungating tumor of the rectosigmoid was found. There were several adjacent, firm, enlarged lymph nodes, but the liver and peritoneal cavity were grossly free of metastases. A one-stage combined abdominoperineal resection of rectum and distal 12 cm. of sigmoid was done. The microscopic diagnosis was adenocarcinoma with twelve of fourteen lymph nodes containing metastatic tumor. The patient was discharged on the twenty-fourth postoperative day with a functioning colostomy and a well-healed perineal wound.

About four months following discharge from the hospital she began to note pain and tenderness over the laterodorsal aspect of the left foot, which made walking uncomfortable. These symptoms increased in severity and became associated with persistent swelling of the dorsum of the left foot together with a mild degree of redness. There was no history of trauma to the extremity, and the patient was well otherwise. She was readmitted to the hospital Feb. 12, 1951, and physical examination at this time revealed her to be in good general health. Examination of the left foot disclosed a moderate degree of pitting edema and redness of the entire dorsum of the foot with exquisite tenderness over the lateral aspect. There were no ulcerations, and the remaining examination of the extremities was negative. Roentgenograms of the foot showed destruction of the left fourth metatarsal, with only the head and neck remaining (Fig. 1).

The other bones of the foot showed a generalized demineralization without localized areas of destruction. Films of the other foot, the skull, thorax, spine, pelvis, and long bones revealed no areas of localized bone destruction.

On Feb. 18, 1951, the lesion of the fourth metatarsal was explored. A semicystic mass was found, largely filled with dark brown fluid and soft, pinkish-gray, pultaceous tissue grossly resembling tumor tissue, which bled profusely. Pathologic report of the biopsied tissue was: metastatic adenocarcinoma, consistent with the site of origin in the rectum (Fig. 3). Comparison of the metastatic tissue with the primary tumor of the rectosigmoid showed many areas wherein the tumor cells were identical.

The biopsy wound failed to heal per primum after six days, and a course of x-ray therapy was begun. Between the dates of Feb. 24, and March 6, 1951, 2,000 r, measured in air, were delivered to each of two 6 by 8 cm. ports covering the dorsal and plantar aspects of the metatarsal, the estimated tumor dose being 3,840 r. At the end of ten days of therapy the pain, tenderness, and swelling had largely subsided. The wound showed almost complete secondary healing on March 8, 1951, and the patient was discharged feeling comfortable and having no other systemic complaints.

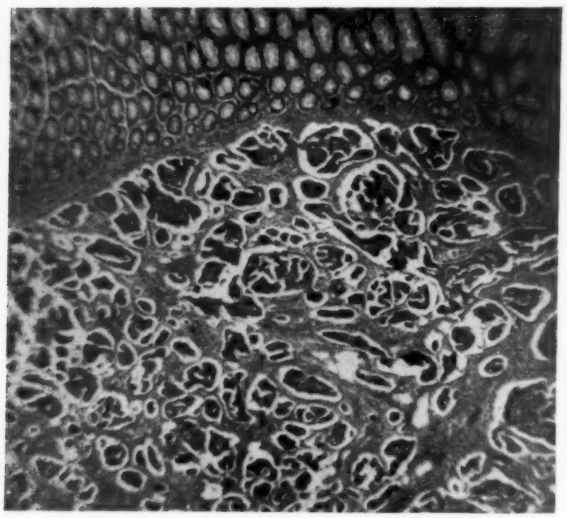

Fig. 2.

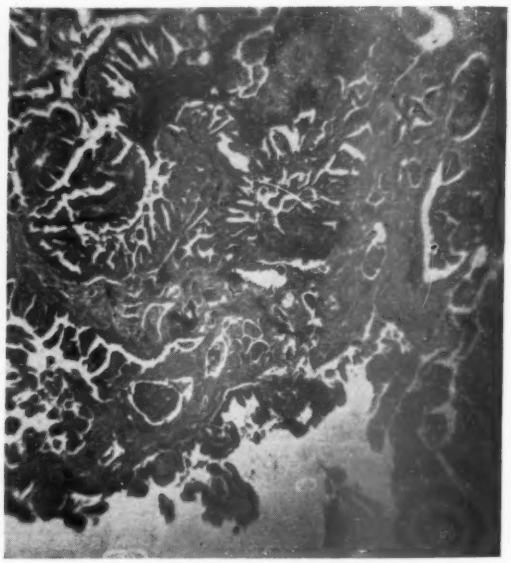

Fig. 3.

Fig. 2.—Low-power photomicrograph of primary carcinoma of rectum showing characteristic papillary adenocarcinoma.

Fig. 3.—Low-power photomicrograph of section of biopsy from metastatic tumor of metatarsal bone showing similarity to primary rectal lesion.

SUMMARY

1. Incidence of bone metastasis from carcinoma of the rectum varies from 0.5 to 10.5 per cent in a review of reported cases in the literature. The vertebrae, pelvis, and ribs are the most common sites. Peripheral bone metastasis is a distinctly rare occurrence and is almost always associated with generalized visceral and skeletal spread.

2. An unusual case is presented of a pathologically proved solitary metastasis to the left fourth metatarsal bone from carcinoma of the rectum, six months postoperatively, in a patient otherwise well.

REFERENCES

1. Abrams, H. L.: Skeletal Metastases in Carcinoma, Radiology **55**: 534, 1950.
2. Aufses, A.: Skeletal Metastases From Carcinoma of the Rectum; Report of Eight Cases, Arch. Surg. **21**: 916, 1930.
3. Bacon, H. E.: Unusual Sites of Metastasis From Carcinoma of the Rectum and Sigmoid Colon, Pennsylvania M. J. **43**: 1573, 1940.
4. Bertin, E. J.: Metastasis to Bone as the First Symptom of Cancer of the Gastrointestinal Tract, Am. J. Roentgenol. **51**: 614, 1944.
5. Brown, C. E., and Warren, Shields: Visceral Metastases From Rectal Carcinoma, Surg., Gynec. & Obst. **66**: 611, 1938.
6. Copeland, M. M.: Bone Metastases: a Study of 334 Cases, Radiology **16**: 198, 1931.
7. Decker, F. H., and Fash, J. C.: Carcinoma of the Rectum With Metastasis to the Tibia, M. Radiog. & Photog. **26**: 125, 1950.
8. Geschickter, C. F., and Maseritz, I. H.: Skeletal Metastases in Cancer, J. Bone & Joint Surg. **37**: 314, 1939.
9. Ghormley, R. K., and Valls, J. E.: Metastasis to Bone From Carcinoma of the Gastrointestinal Tract, J. Bone & Joint Surg. **37**: 74, 1939.
10. Hubeny, M. J., and Mass, M.: Roentgenologic Aspects of Metastases, Radiology **35**: 315, 1940.
11. Johnson, E. W., Jr., and Janes, J. M.: Metastatic Adenocarcinoma of the Talus From the Recto-sigmoid Area, J. Bone & Joint Surg. **31 A**: 181, 1949.
12. Stein, J.: Metastasis to Bone From Carcinoma of the Gastrointestinal Tract, Radiology **35**: 486, 1940.
13. Weston, S. D.: Metastasis to the Humerus From Carcinoma of the Rectum, Am. J. Surg. **57**: 531, 1942.

INTUSSUSCEPTION OF ILEUM THROUGH PERSISTENT OMPHALOMESENTERIC DUCT

Review of the Literature and Report of Two Cases

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ALTHOUGH anomalies resulting from faulty or incomplete obliteration and disappearance of the embryologic omphalomesenteric duct are relatively common, complete patency of the duct is quite rare. Kittle, Jenkins, and Dragstedt,[23] who collected 104 uncomplicated cases from the literature, reported that complete patency of the omphalomesenteric duct occurred in only two infants in over 30,000 births at the Chicago Lying-in Hospital.

The most serious complication resulting from complete patency of the omphalomesenteric duct is the intussusception or prolapse of ileum through the duct onto the abdominal wall, leading ultimately, in untreated cases, to strangulation and gangrene of the involved intestine. Peake,[28] in 1811, was the first to describe this unusual occurrence. The excellent reviews of this subject by Cullen[11] and Kittle, Jenkins, and Dragstedt[23] include summaries of thirty cases[1, 3-5, 7, 9, 10, 12-33] which had appeared in the literature up to 1947. Three additional cases have subsequently been described by Clark,[8] Bronaugh,[6] and Arnheim.[2]

Twenty-two of the thirty-three cases were reported prior to 1900. All of the reports have been of single cases with the exception of the description in 1885 of two cases by Théremin.[30] Owing to rarity of this condition and the very few reported instances of its successful treatment we feel it advisable to report two cases recently treated by operative reduction of the intussusception and resection of the persistent omphalomesenteric duct.

CASE REPORTS

Case 1.—The patient was a 6-day-old white male infant who was admitted to the hospital on Nov. 28, 1949, for study because of known congenital heart disease. He had been born by cesarean section and weighed 7 pounds and 2 ounces at birth. He had experienced considerable respiratory difficulty during his first six days of life and the existence of other congenital anomalies in addition to congenital heart disease was suspected. Physical examination at the time of admission was essentially within normal limits except for the presence of a left facial paralysis and a loud systolic mumur over the left precordium. Examination of blood and urine revealed relatively normal findings.

The patient suffered from progressive respiratory difficulty necessitating continuous oxygen therapy and frequent aspirations of the nasopharynx. Mild cyanosis was occasionally noticed. Roentgenographic examination of the chest revealed evidence of marked cardiac enlargement.

On December 21, the discharge of fecal material from a previously normal-appearing umbilicus was first noticed. This discharge continued, with excortication of the adjacent

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abdominal wall, until December 27, the infant's twenty-ninth day of life, when approximately 10 cm. of mucosal-covered, inverted small bowel suddenly prolapsed through the umbilicus onto the abdominal wall (Fig. 1).

The patient was immediately taken to the operating room, and under Vinethene-ether anesthesia a circular incision was made around the protruding bowel, including a small rim of skin. The incision was continued down to the peritoneum and the involved intestine was freed. On examination it was discovered that an intussusception of ileum into a persistent omphalomesenteric duct had occurred. The intussusception was easily reduced, the omphalomesenteric duct was excised, and the defect in the ileum was closed transversely with interrupted inverting sutures of fine silk. The wound was approximated in layers with interrupted fine silk sutures. The infant tolerated the procedure well. However, the patient's previous respiratory distress continued postoperatively. His respiratory excursions became increasingly rapid and shallow. His cyanosis increased, and he expired on December 29.

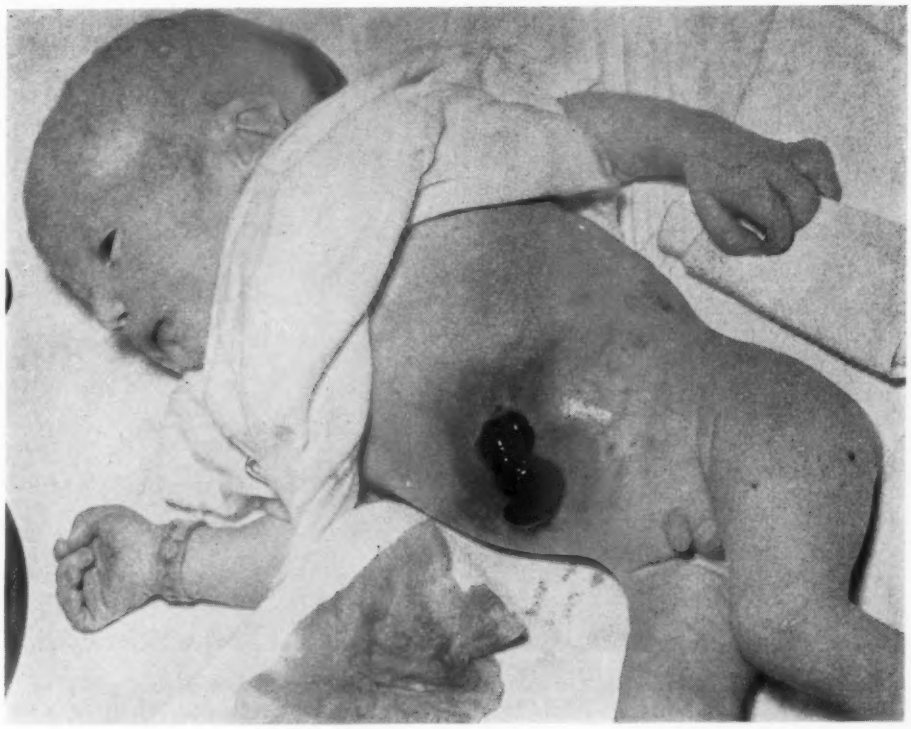

Fig. 1.—Photograph showing the prolapsed ileum in Case 1.

On post-mortem examination, the heart was found to be considerably enlarged. The right ventricle was two to three times larger than the left ventricle and the right auricle was greatly distended. There was a large anomalous communication between the aorta and the main pulmonary trunk just distal to the base of the heart. The ductus arteriosus and the foramen ovale were widely patent. The left superior vena cava had persisted and communicated with the right atrium by way of the coronary sinus. Microscopic examination of the lungs revealed bilateral patchy intra-alveolar hemorrhage. The closure of the ileum was intact and there was no evidence of peritonitis. Congenital heart disease with cardiac failure was regarded as the cause of death.

Case 2.—The patient was a 12-day-old white male infant who was admited to the hospital on Jan. 28, 1951, for treatment of a mucosal-covered mass which had prolapsed through the umbilicus onto the abdominal wall eleven hours prior to admission. The parents stated

that the infant first passed fecal material through the region of the umbilicus at 7 days of age when the umbilical cord sloughed away. Although small amounts of feces were passed through the umbilicus, the bulk of the feces was excreted by rectum. Since the first protrusion of the mass onto the abdominal wall, it had become progressively larger and darker in color. The infant had vomited once, shortly after the prolapse.

On physical examination, an edematous, dark red, mucosal-covered, T-shaped mass measuring approximately 12 by 6 by 6 cm. was seen to be protruding from the region of the umbilicus (Fig. 2,*A*). Both ends of the T-shaped mass were open and presumbly represented inverted small bowel. The physical examination was otherwise normal. The temperature and laboratory findings were within normal limits. The patient's weight was 7 pounds and 8 ounces.

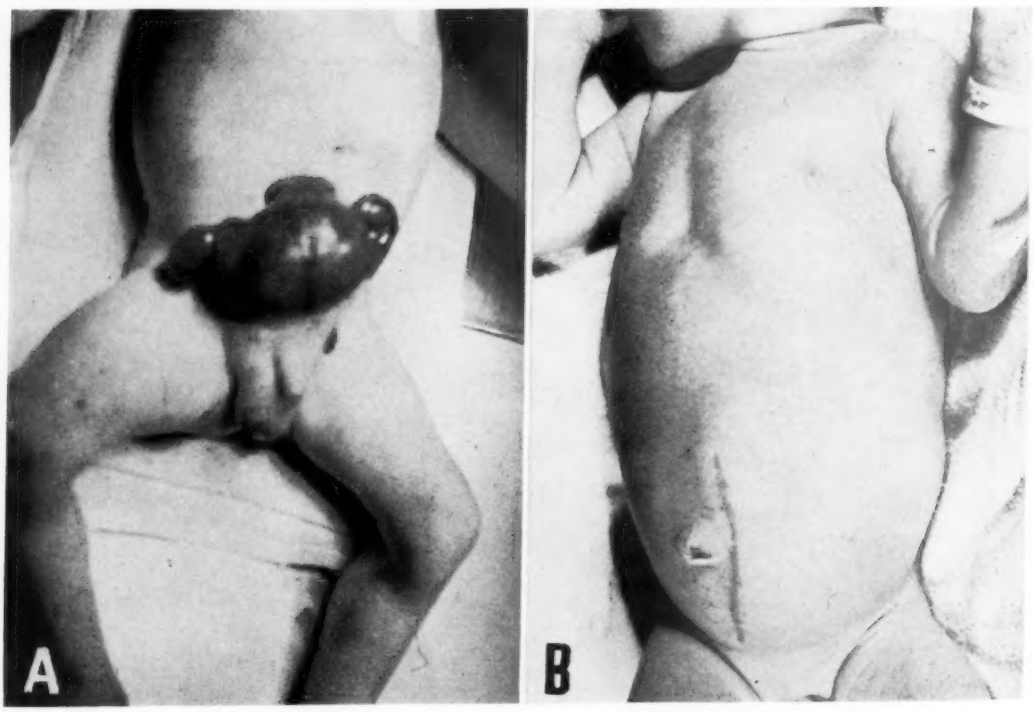

Fig. 2.—Photographs showing (*A*) the prolapsed ileum before operation in Case 2 and (*B*) the abdominal wall after surgical repair.

The patient was operated upon one hour after admission under Vinethene-ether anesthesia. The peritoneal cavity was entered through a mid-left rectus incision. It was discovered that both afferent and efferent segments of ileum had intussuscepted through a persistent omphalomesenteric duct (Fig. 3). The mass was freed by a circular incision through the junction of the skin and the inverted omphalomesenteric duct. The distal portion of the omphalomesenteric duct was incised to permit the disinvagination of the involved ileum. Both ileal segments appeared viable although there was some dilatation of the ileum in the area of the origin of the omphalomesenteric duct. The omphalomesenteric duct was excised and the defect in the ileum was closed with interrupted, inverting fine silk sutures. The small defect in the umbilical region was closed in layers with silk sutures preserving the appearance of an umbilicus, and the left rectus incision was similarly closed in layers with interrupted sutures of fine silk.

The postoperative course was completely uneventful. Gastric suction by means of a Levine tube was maintained during the early postoperative period and parenteral feedings

were carried out through a small polyethelene tube inserted into an ankle vein. The patient received penicillin, sulfadiazine, and streptomycin postoperatively. When the patient was discharged from the hospital on February 5, he was taking his formula well and was having normal bowel movements.

The infant was seen several times in the outpatient department and appeared to be doing nicely. He was gaining weight and his wounds were well healed (Fig. 2, *B*).

He was readmitted on March 7 for treatment of an early high small intestinal obstruction. He was operated on shortly after admission and a mechanical obstruction of the jejunum due to adhesive bands was released by division of the adhesions. The postoperative course was again uncomplicated and the patient was discharged on April 6, weighing 11 pounds and 4 ounces. The hospital stay was prolonged in order to give the infant ACTH in an effort to reduce the likelihood of subsequent difficulty from reformation of intraperitoneal adhesions. The patient has done well since discharge.

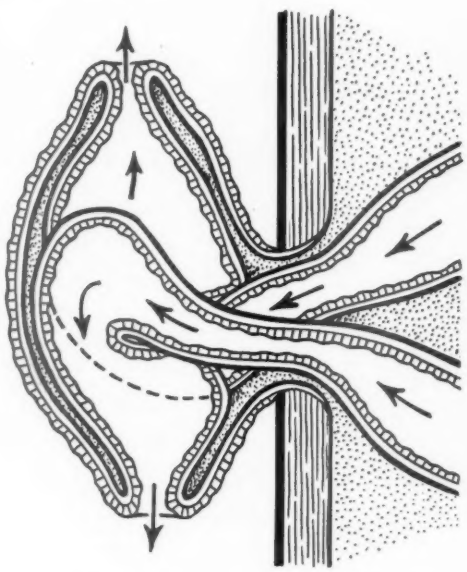

Fig. 3.—Diagrammatic drawing of the intussusception in Case 2.

DISCUSSION

The sex distribution of infants suffering from intussusception of ileum through patent omphalomesenteric duct is predominantly male. Information concerning the sex of the patients is available in twenty-eight of the thirty-five reported cases, including our two cases. Twenty-six were male while only two were female. The same tendency toward male predominance, although to a lesser degree, is to be observed in the uncomplicated cases of patent omphalomesenteric duct summarized from the literature by Kittle, Jenkins, and Dragstedt. Of the eighty-three cases in which the sex was given, seventy-one were male and twelve were female. Thus, 87 per cent of the patients with persistent omphalomesenteric ducts reported in the literature have been male.

The ages of the infants at the time of the prolapse are of interest. The time of this occurrence has ranged from birth to 7 months of age, the majority of such episodes occurring in the first four weeks of life (Table I). The time

interval from the first appearance of fecal drainage in the umbilical area to the intussusception of the ileum onto the abdominal wall is known in twelve cases and ranged from 5 days to 7 months (Table II).

TABLE I. AGE OF THE PATIENTS AT THE TIME OF PROLAPSE

AGE AT TIME OF PROLAPSE	NUMBER OF CASES
Under 7 days	4
1 to 4 weeks	20
1 to 6 months	10
Over 6 months	1

TABLE II. TIME INTERVAL FROM THE APPEARANCE OF A FECAL FISTULA TO PROLAPSE

INTERVAL	NUMBER OF CASES
1 to 7 days	5
1 to 4 weeks	4
1 to 7 months	3

The therapeutic results, until recently, have been most discouraging. In thirteen cases no effort was made to correct the intussusception surgically. All of these patients died although there was a question of spontaneous reduction and limited survival in two of them.[22, 30]

Various operative measures were carried out in twenty-two cases, including simple incision of the umbilical ring in an effort to effect a reduction of the intussusception, reduction of the intussusception and excision of the omphalomesenteric duct with closure of the ileal defect, and occasionally resection of nonviable ileum with the omphalomesenteric duct. Cutler[12] described, in 1924, a case treated by reduction of the prolapse and excision of the omphalomesenteric duct, which survived long enough to be discharged from the hospital nine days postoperatively but died a short but unspecified time later. The first long-term postoperative survival was reported in 1947 by Kittle, Jenkins, and Dragstedt.[23] Their case had been operated upon in 1943 by Dr. Dragstedt and a resection of the intussuscepted mass and a side-to-side ileal anastomosis had been carried out. In 1947, Bronaugh[6] described a successful resection of nonviable ileum and omphalomesenteric duct with end-to-end ileal anastomosis and in 1950, Arnheim[2] discussed a successful case in which 4 cm. of ileum had been resected with the persistent duct, followed by a side-to-side ileal anastomosis. Death occurred in all of the other cases treated by operation.

The appallingly high reported mortality (89 per cent) associated with this condition is misleading, since most of the cases were treated before the development of modern surgical techniques and contemporary concepts of pre- and postoperative care. It is significant that only one death has occurred in the five operative cases, including our own, reported since 1947, and that the single death among these resulted from congenital heart disease rather than from factors associated with the operative procedure. Future results in the treatment of intussusception through a persistent omphalomesenteric duct

should be much improved with early surgical intervention, our safer modern anesthesia, and the judicious use of such measures as gastric suction, parenteral fluid therapy, and antibiotics.

SUMMARY

1. Two cases of intussusception of ileum through a persistent omphalomesenteric duct have been presented. In both cases the intussusception was reduced and the omphalomesenteric duct was excised. One infant survived while the other died in the early postoperative period as the result of severe preexisting cardiac failure, secondary to congenital heart disease.

2. Thirty-five cases from the literature, including our two cases, have been analyzed with certain conclusions:

(a) Ileal intussusception through a persistent omphalomesenteric duct occurs predominantly in male infants.

(b) The intussusception most commonly takes place during the first four weeks of life and is often preceded for several days by the development of a fecal fistula in the region of the umbilicus.

(c) The over-all mortality of 89 per cent is misleading since most of the cases were reported prior to the development of modern therapeutic methods.

(d) The recently reported cases reveal a marked reduction in mortality.

3. The importance of early operative intervention and active supportive measures is emphasized.

REFERENCES

1. Arndt, C.: Ein Fall von Dünndarmprolaps durch den offen gebliebenen Ductus omphalomesentericus, Arch. f. Gynaek. **52**: 71, 1896.
2. Arnheim, E. E.: Surgical Complications of Congenital Anomalies of the Umbilical Region, Surg., Gynec. & Obst. **91**: 71, 1950.
3. Barth, A.: Ueber die Inversion des offenen Meckel'schen Divertikels und ihre Complication mit Darmprolaps, Deutsche Ztschr. f. Chir. **26**: 193, 1887.
4. Basevi, S.: Jahrb. f. Kinderh. **12**: 275, 1878.
5. Blin, L.: Diverticulum de l'intestin ileum chez un infant de 6 mois; anus contre natura à la ombilic, issue d'une anse intestinale par l'orifice ombilical; étranglement; débridement; mort; autopsie, Mém. de la Soc. de biol., Paris 1. sér. **4**: 131, 1853.
6. Bronaugh, W.: Herniation and Exstrophy of the Ileum in the Newborn Incidental to Adherent Meckel's Diverticulum in the Umbilical Area, West Virginia M. J. **43**: 126, 1947.
7. Clamann, M.: Ductus omphalo-entericus persistens, Deutsche med. Wchnschr. **28**: 416, 1902.
8. Clark, D. V.: Extrophy of the Ileum Through a Patent Omphalomesenteric Duct With Strangulated Umbilical Hernia, J. Internat. Coll. Surg. **9**: 251, 1946.
9. Cooper, P. R.: Extroversion of the Bowel Through an Umbilical Faecal Fistula, Due to a Patent Meckel's Diverticulum, Clin. J., Lond. **47**: 78, 1918.
10. Cserey-Pechany, A.: Zwei Fälle van totaler Nabelfistel, Zentralbl. f. Chir. **69**: 795, 1942.
11. Cullen, T. S.: Embryology, Anatomy, and Diseases of the Umbilicus Together With Diseases of the Arachus, Philadelphia, 1916, W. B. Saunders Company.
12. Cutler, G. D.: Prolapse of the Bowel Through a Patent Omphalomesenteric Duct Opening on the Side of the Umbilical Cord, Boston M. and S. J. **190**: 782, 1924.
13. Gesenius, H.: Inversion des Dünndarmes durch ein am Nabel offen gebliebenes Divertikel, J. f. Kinderkrankh. **30**: 56, 1858.
14. Gevaert, G.: Inversion intestinale à travers l'ombilic, in Charon et Geraert: Chirurgie Infantile, ed. 2, Bruxelles, 1895, p. 251.
15. Gibb, G. D.: Unique Congenital Malformation Associated With Umbilical Hernia and a Pendulous Artificial Anus, Tr. Path. Soc. Lond. **7**: 216, 1856.
16. Golding-Bird, C. H.: A Case of Intussusception Through a Patent Meckel's Diverticulum, Tr. Clin. Soc., Lond. **29**: 32, 1896.

17. Guthrie, L. G.: A Case of Patent Meckel's Diverticulum Into Which the Posterior or Distal Wall of the Ileum Became Intussuscepted, Forming an Umbilical Tumor. Pediatrics **2**: 1, 1896.
18. Helweg, K.: Aabent Diverticulum ilei; Invagination, Prolaps, Inkarceration, Hosp. Tidende **2**: 705, 1884.
19. Holmes, T.: Surgical Treatment of the Diseases of Infancy and Childhood, London, 1868, p. 182, Longman.
20. Hue, F.: Prolapsus ombilical diverticulaire, Normandie méd. **21**: 162, 1903.
21. Hüttenbrenner, A.: Allg. Wien. med. Ztg. **23**: 225, 1878.
22. King, T. W.: Faeculent Discharge at the Umbilicus From Communication With the Diverticulum Ilei, Guy's Hosp. Rep. 2 s. **1**: 467, 1843.
23. Kittle, C. F., Jenkins, H. P., and Dragstedt, L. R.: Patent Omphalomesenteric Duct and Its Relation to the Diverticulum of Meckel, Arch. Surg. **54**: 10, 1947.
24. Kölbing, A.: Beschreibung einer auf dem Nabel eines neugebornen Kindes befindlichen röthlichen Geschwulst, besonders wegen ihrer Folgen merkwürdig, Neue Ztschr. f. Geburtsk **14**: 443, 1843.
25. Löwenstein, L.: Der Darmprolaps bei Persistenz des Ductus omphalo-mesentericus, mit Mittheilung eines operativ geheilten Falles, Arch. f. klin. Chir. **49**: 541, 1894-95.
26. Most, A.: Offener Ductus omphalo-entericus und Nabelschnurbruch, Beitr. z. klin. Chir. **144**: 236, 1928.
27. Ophüls, W.: Beiträge zur Kenntnis der Divertikelbildungen am Darmkanal, Inaug. Dissert. s. 36, Göttingen, 1895.
28. Peake, J.: Case of Preternatural Anus Found in a Portion of Ileum Protruded at the Umbilicus, Edinburgh M. & S. J. **7**: 52, 1811.
29. Siebold, A.: in Schröder, G.: Ueber die Divertikel-Bildungen am Darm-Kanale, Inaug. Dissert. (Erlangen), Augsburg, 1854.
30. Théremin, E.: Sur les fistules entéro-ombilicales diverticulaires, Rev. mens. d. mal. de l'enf. **3**: 554, 1885.
31. Veit, K. E.: Zur Kenntnis des Offenbleibens des Ductus omphalomesentericus, Arch. f. klin. Chir. **102**: 1014, 1913.
32. Violbing, J.: in Bureau, J.: Prolapsus ombilical du diverticule de Meckel, Thèse de Paris, No. 257, 1898.
33. Weinlechner, J.: Vorfall des Dünndarms durch den offen gebliebenen Ductus omphalomesaraicus, Jahrb. f. Kinderh., N. F. **8**: 55, 1874-75.

SOLITARY MYELOMA OF RIB SIMULATING MEDIASTINAL TUMOR

Report of a Case

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INTEREST has been directed toward cases of solitary myeloma of bone for the past twenty years, but remarkably few cases have been reported or confirmed during that time. A review of the literature indicates that the term "solitary myeloma" is properly applied only to those cases in which a single myeloma has remained the sole lesion for an extended period. Some authors believe these lesions are of benign character and that they remain inactive over long periods of time. It is not the purpose of this communication to review the entire literature on the subject for this has been well done previously by Cutler, Buschke, and Cantril,[3] Aufses,[1] and Geschickter and Copeland.[4] A recent case has been reported by Nassim and Crawford.[6]

It is interesting to note that only three cases of solitary myeloma of rib have been reported to date, one by Aufses[1] and two by Jones.[5] In a critical analysis by Bichel and Kirketerp[2] the following criteria were established for the diagnosis of solitary myeloma: (a) repeatedly negative sternal biopsies, (b) negative bone x-ray studies, (c) definite pathologic diagnosis, (d) long period of observation without generalized spread for cases reported while still living, and (e) microscopic examination of the entire skeleton at necropsy. As noted by Aufses, solitary myeloma must by such criteria be an exceptionally rare disease, and one of continuing interest.

The following case is presented, inasmuch as it meets all of Bichel and Kirketerp's criteria except necropsy which was denied, and also because it presents an interesting type of myelomatous disease simulating mediastinal tumor. The prior excellent health of the patient, the sudden incapacity due to massive hydrothorax, the size of the lesion, and the persistent negative bone roentgenograms and sternal biopsies present a somewhat different picture than those previously reported.

CASE REPORT

A white woman, aged 64 years, was admitted to Marion City Hospital† on May 14, 1949, complaining only of dyspena and orthopnea of three weeks' duration. She presented no other complaints. She was first seen by her physician three days prior to admission, at which time a diagnosis of congestive heart disease was made on the basis of her complaint and an apparent peripheral edema. History revealed a gradually increasing dyspnea over the three weeks' period, but no evidence of marked swelling of the extremities. There had been no antecedent illness, and no complaint of fever, chills, respiratory infection, cough,

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pain, hemoptysis, or change in general body functions. She had always enjoyed good health and denied any major illness, surgical operation, or hospitalization. Family history was remarkable only for longevity. She was seen again at home by her physician on May 14, at which time he noted a marked shift of the mediastinum and heart to the left, with flatness to percussion over the entire right chest and absent breath sounds. On admission to hospital the same day he performed right thoracentesis, and aspirated 3,500 c.c. of slightly blood-tinged amber fluid. However, the remaining fluid level still obscured the right lung field on x-ray examination, and he made further unsuccessful attempts to evacuate the pleural cavity. Bacteriologic and pathologic studies of the fluid showed no evidence of infection or tumor cells. I was called in consultation on May 19, 1949, and the case was subsequently transferred to my surgical service.

Examination.—Physical examination showed an obese woman with no gross evidence of illness or weight loss, resting quietly in bed without undue respiratory distress. Temperature was 36.8° C., pulse 80, respiration 20, blood pressure 118/80, height 66 inches, and weight 190 pounds. Physical findings relative to the head, neck, extremities, abdomen, pelvis, and rectum were normal. Neurological examination was not contributory. The trachea was shifted toward the left and the apical cardiac impulse was in the left mid-axillary line. The right lung field was noted to have a fluid level to the fourth rib posteriorly, with flat percussion note over the entire chest below this level, and with absent breath sounds. Distant breath sounds were noted above the level of the fourth rib. Excursion of the chest was limited on the right. The diaphragm could not be identified for position or motion. Heart sounds, rate, and rhythm were normal. Roentgenograms taken on May 14 and 15 were reviewed, and for the most part revealed only the massive right hydrothorax and mediastinal shift to the left. Blood findings were: hemoglobin 12.4 Gm., red cells 4.7 million, white cells 17,000 (polymorphonuclears 90 per cent, lymphocytes 8 per cent, monocytes 2 per cent). Kahn-Kline serology test was negative. Urine was clear, acid, specific gravity 1.035, albumin negative, sugar negative; microscopic examination showed scattered pus cells only. Pleural fluid: specific gravity 1.02; culture, no growth; smears, no organisms; pathologic study, no tumor cells. Electrocardiography was normal. (Bence-Jones protein test was not done at this time.)

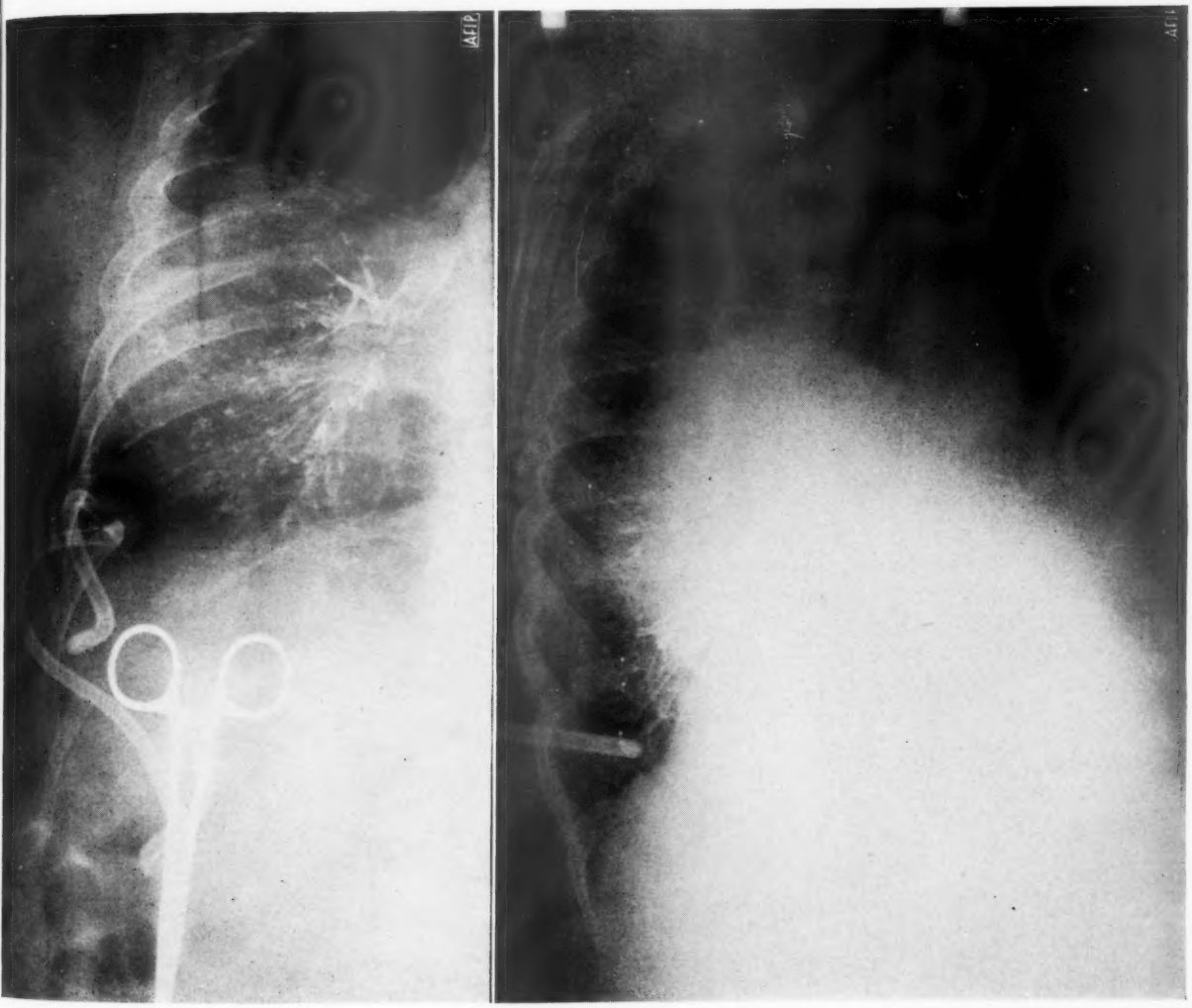
During the period May 20 to 24, repeated efforts were made to aspirate completely the right pleural cavity without success. Finally on May 25 the patient was taken to the operating room where trochar and catheter drainage was established and the pleural cavity drained in stages.

Roentgenograms were then taken which demonstrated a large tumor mass in the lower right pleural cavity, which was interpreted by the roentgenologist as a large pulmonary cyst. The description was as follows: An opaque, round, sharply-outlined, soft tissue mass was present in the lower half of the right lung anteriorly. This measured approximately 13 cm. in diameter. It obscured the right cardiac border and the medial half of the right diaphragm. A streak of increased density was present, superior to the mass. This was probably a small area of atelectasis. The rest of the lung fields were clear. The mediastinum was in normal position. The impression was a soft tissue mass, right lung, probably a pulmonary cyst.

This diagnosis was not concurred in by me, however, and on May 26, bronchograms were made which revealed the mass to be extrapulmonary (Fig. 1). This mass appeared to arise from the mediastinum and could not be projected away from the area on the chest wall in fluoroscopic examination or oblique x-rays. The roentgenologist however, still believed the mass to be a pulmonary cyst in the right middle lobe. A diagnosis of anterior mediastinal tumor, probably dermoid, with intrapleural projection was made by me following consideration of the various possibilities. Rib structure beneath the tumor mass could not be made out on the roentgenograms. The patient was prepared for surgical operation.

Operation.—On May 27, right thoractomy was performed under endothracheal anesthesia, using a posterolateral approach and resecting the seventh rib subperiosteally. A large, 12 by 8 cm. (420 Gm.) dull red, friable, encapsulated tumor mass was found arising from the anterior portion of the thorax in the region of the fourth and fifth ribs. There was no

distinct pedicle, but dissection revealed that the tumor arose from the fifth rib, which was almost completely replaced by the lesion over a distance of 5 to 6 cm. The entire tumor together with the involved rib was resected. The mass nearly filled the lower pleural cavity, but there was no fixation by adhesions or extension, and the lung was normal, although compressed. A section of the fourth rib was also taken and dissection carried well into the subpectoral space. The patient's postoperative course was uneventful, and the drainage tube was removed in forty-eight hours. A slight hydrothorax developed, which was completely removed by two thoracenteses and did not recur. A postoperative diagnosis was made of probable sarcoma.



A. *B.*

Fig. 1.—*A*, Posteroanterior roentgenogram of right chest, Lipiodol bronchogram, showing the tumor mass and adjacent normal lung structure. *B*, Oblique views further demonstrating the tumor mass and lung.

Pathologic Examination.—When the pathologist* reported the tissue, however, he made a diagnosis of multiple myeloma with typical amyloid deposits. The pathologic report in detail: Sections displayed a mixed picture including some areas of neoplasia, large areas of necrosis and hemorrhage, extensive inflammatory response to hemorrhage and necrosis,

*Dr. Horace B. Davidson.

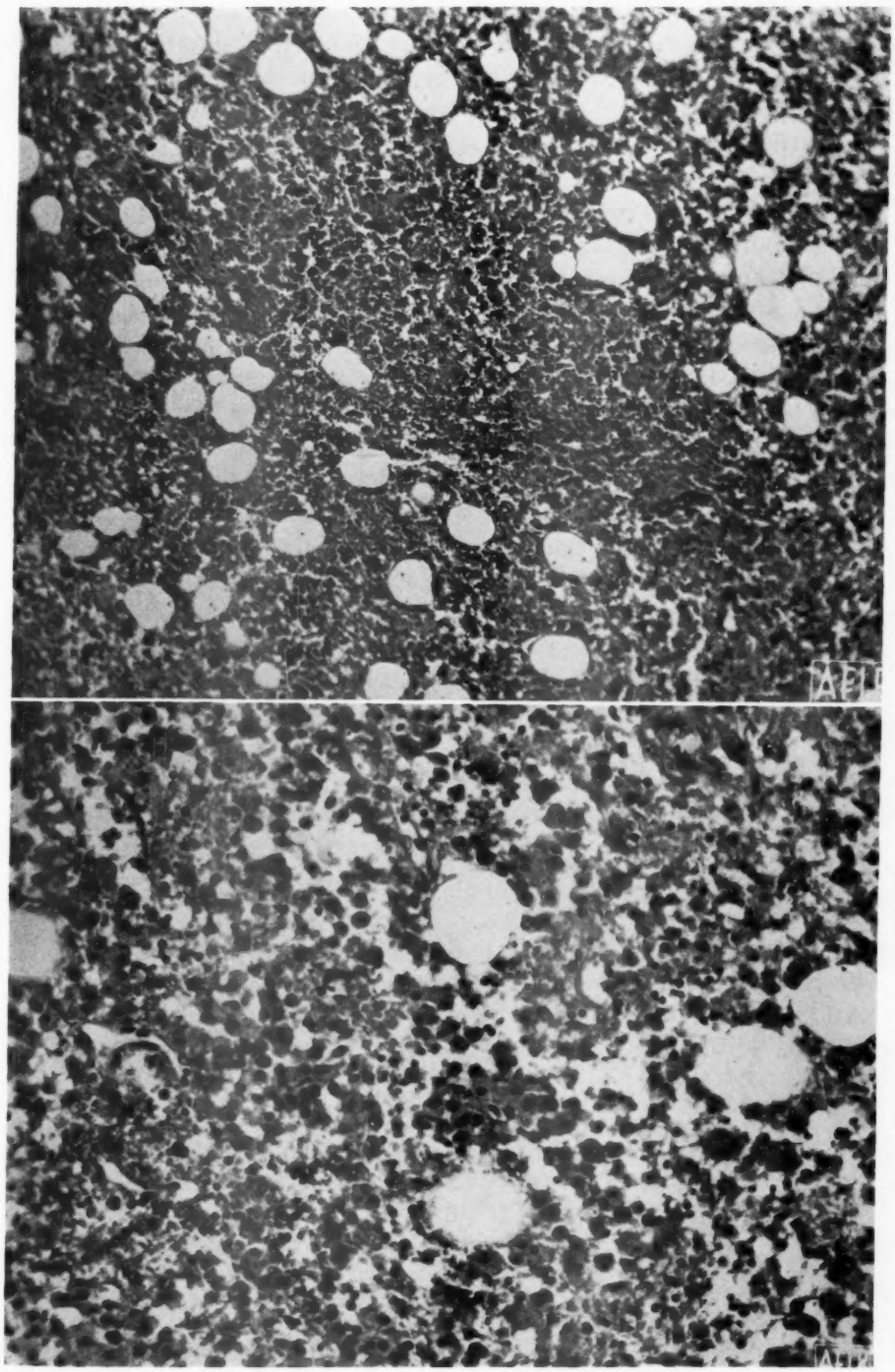
and large masses of material appearing to be amyloid deposits. The neoplastic pattern was fairly constant in areas of necrosis and was characterized by fairly closely packed, uniform-appearing cells with a rather abundant, somewhat vacuolated, moderately eosinophilic cytoplasm, and eccentric nuclei with prominent spoke-like distribution of chromatin. At times these cells had several nuclei. They could be fairly definitely identified as plasma cells. The accompanying hemorrhage necrosis and inflammatory response were more or less expected in this type of tumor. The unusual feature was in the form of large amorphous masses of pink material histologically appearing to be amyloid. In many areas there were multinucleated foreign body giant cells around such masses. Diagnosis was multiple myeloma with atypical amyloid deposits (Fig. 2). The diagnosis of myeloma was confirmed by subsequent and more detailed studies by the pathologist. X-ray studies on the skeleton were then made which failed to reveal any other evidence of the disease. Sternal biopsy was normal. There was no Bence-Jones protein in the urine. The diagnosis of the case was therefore changed to solitary myeloma of the rib. The patient was discharged from the hospital on June 13, 1949, in good condition.

Follow-up.—Following discharge from hospital, the patient was given a full course of deep x-ray therapy to the right chest region and had no severe irradiation effects. She was seen at weekly intervals for three months, biweekly for two months, and thereafter at monthly intervals until September, 1950. During this period her weight remained constant, she carried on her usual household activities, and claimed good health. Repeated bone check by x-ray failed to reveal any evidence of other bony lesions. Sternal biopsies on June 28, 1950, and Sept. 7, 1950, showed only mild hyperplasia without significant plasma cells. Chest x-ray examination revealed no evidence of recurring lesion in the chest wall, nor recurrence of hydrothorax. I last saw the patient on Sept. 19, 1950, at which time she was referred to a medical associate for further observation, since she was complaining of back pain and abdominal swelling, and I was leaving the city for an extended period.

She was readmitted to hospital on September 20, where abdominal paracentesis produced 6,000 c.c. of slightly cloudy amber fluid. Pathologic study of the fluid demonstrated no tumor cells. There was an anemia of 67 per cent hemoglobin and red cells of 2.98 million, with white elements of 9,350. Blood urea nitrogen was 19.7 mg. Bence-Jones protein was negative. The physician felt that she had developed abdominal metastasis although this could not be proved. On October 5 she was readmitted for study following further deep x-ray therapy. There was pitting edema of the lower extremities, blood pressure 150/90, and recurrence of abdominal fluid following the x-ray therapy. General examination was not remarkable except for the distended abdomen, and the blood and urine pictures were essentially unchanged. Aspiration again produced 6,000 c.c. of clear fluid which failed to reveal pathologic cells on study. She was transfused twice and discharged.

Her last admission was Oct. 29, 1950, when she was readmitted for further blood transfusions and study. In the interval since previous hospitalization she had felt well, appreciably stronger and able to carry on her house work. She had continued to receive x-ray therapy. General examination was still within normal limits. The chest was clear and examination of the bony structure normal. Blood examination showed the persistent low-grade anemia, but urine examination was normal, and blood urea nitrogen 17 mg. She was given four blood transfusions, the last on November 2, following which she had a severe chill and became semicomatose. Her temperature remained normal, but she developed clinical icterus, ecchymosis, decreased urine output and blood urea nitrogen rose to 47 mg. On November 7 she developed convulsions, became completely comatose, and died. A final diagnosis of solitary myeloma of rib with probable abdominal metastasis with ascites, hypochromic anemia, and terminal hepatorenal failure was made by the physician. Transfusion reaction with complicating lower nephron syndrome could not be excluded. Permission for autopsy was urged, but the family refused this examination despite the excellent reasons advanced.

A.



B.

Fig. 2.—*A*, Low power photomicrograph and *B*, high power photomicrograph of the pathologic specimen, showing the plasma cells and abundant amyloid tissue.

COMMENT

Review of the literature indicates that cases of solitary myeloma are rare, and involvement of a rib even more unusual. The case presented has satisfied the criteria of Bichel and Kirketerp except for the performance of necropsy and the microscopic study of the skeleton. The exact diagnosis in this case was not made until after surgical excision and pathologic study of the specimen, for previous studies, roentgenograms, and the appearance of the mass did not suggest its true nature. The size of the tumor would indicate that it had existed over an extended period of time in spite of the very brief duration of symptoms and the apparent tolerance until the onset of ever increasing hydrothorax. This would tend to support the belief that the myelomatous disease was indeed solitary and that the duration was much longer than the known interval between diagnosis and death. It is believed that this case does present a true solitary myeloma of rib even though it was not possible to obtain autopsy material for final investigation. Throughout the period of study and observation sternal biopsies, x-rays, and other cellular examinations failed to reveal the existence of any other than the primary rib tumor. The case would seem to refute the view propounded by Cutler and others that solitary myelomas are benign in nature in contrast to cases of multiple disease. It is true, of course, that the period of postoperative observation lasted but eighteen months, which period may be too short to permit acceptance that general bone marrow spread would not have occurred. Metastasis to the abdomen with ascites was suspected, but not confirmed. However, the rib remained as the sole primary lesion.

SUMMARY

1. An unusually large solitary myeloma of rib is presented and added to the limited literature on the subject. It is especially interesting in that it simulated a large mediastinal tumor, and was further thought by the roentgenologist to be a pulmonary cyst.

2. It is believed that this case represents a true instance of solitary myeloma of rib in view of the pathologic study of the original tumor, the negative x-ray examinations over eighteen months' time, the persistently negative sternal bone marrow biopsies, and the fairly long period of observation without evidence of generalized bony spread.

REFERENCES

1. Aufses, A. H.: Solitary Myeloma of a Rib, J. Mt. Sinai Hosp. **15**: 150, 1948.
2. Bichel, J., and Kirketerp, P.: Notes on Myeloma, Acta radiol. **19**: 487, 1938.
3. Cutler, M., Buschke, F., and Cantril, S. T.: The Course of Single Myeloma of Bone, Surg., Gynec. & Obst. **62**: 918, 1936.
4. Geschickter, C., and Copeland, M.: Multiple Myeloma, Arch. Surg. **16**: 807, 1928.
5. Janes, R. M.: Primary Tumors of Ribs, J. Thoracic Surg. **9**: 145, 1939.
6. Nassim, J. R., and Crawford, T.: Solitary Myeloma with Generalized Metabolic Disturbance, Brit. J. Surg. **37**: 287-91, Jan. 1950.

RUPTURE OF THE NORMAL ESOPHAGUS

Report of a Case With Recovery Following Unusual Complications

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RUPTURE of the apparently normal esophagus may result from violent vomiting or severe coughing. Recovery from this usually lethal accident has been reported infrequently and only in recent years.[2-4, 7-9, 11-15] The case reported below indicates the course of a patient who was denied the conventional early surgical therapy because of an existing blood dyscrasia, and further suggests that conservatism may lead to disastrous results.

CASE REPORT

F. G., a 55-year-old white farmer, was admitted to Kennedy Hospital at 2:15 P.M. Dec. 5, 1950. About 7 A.M. the day of admission the patient had a paroxysm of coughing after breakfast, a not unusual occurrence for him. During the coughing, there was sudden, severe, sharp pain in the lower posterior chest bilaterally with radiation "into the top of his head." Immediately thereafter, he vomited a small amount of "tan" fluid. He became extremely weak, and was assisted to bed. The pain was continuous, aggravated by deep breathing and movement. A physician found the blood pressure to be "70," administered a "large" dose of morphine and advised hospitalization. The opiate lessened the pain very little and the patient developed severe thirst during the trip to the hospital, a distance of 115 miles.

During a previous admission in 1947, he had been found to have a hemorrhagic disorder of an obscure type, resembling familial purpura simplex. This was manifested by development of ecchymotic areas beneath the skin either spontaneously or subsequent to mild trauma. The ecchymoses appeared infrequently, were never disabling. Treatment with rutin resulted in improvement, therapy being continued following discharge. The patient was advised against future operation unless no other possible form of therapy could be employed. The past history was not otherwise significant.

Physical Examination.—Physical examination revealed an acutely ill, pale, slightly cyanotic, dyspneic white man complaining of severe posterior chest pain. Oral temperature was 97° F., pulse 136 per minute, and respirations 44 per minute. Purpuric areas were noted on the right upper arm. The right external jugular vein was markedly prominent. Breathing was rapid, shallow, and associated with groaning. Percussion note was dull and breath sounds were diminished over both lung bases. Rhonchi and râles were audible over both lung fields. Blood pressure was 120/70. The heart was not enlarged. No cardiac murmurs were heard. The abdominal muscles were very tense, making accurate palpation difficult. Generalized abdominal tenderness was noted. Peristaltic sounds were not heard. Rectal examination revealed a tan stool and a slightly enlarged prostate.

Laboratory Findings.—White blood count was 7,300, neutrophils 75 per cent, lymphocytes 13 per cent, monocytes 12 per cent, red blood count was 5,300,000, hemoglobin 15.1 Gm., hematocrit 48 per cent. Urine pH 4.5, specific gravity 1.020, albumin trace, sugar negative, microscopic sediment contained a rare white blood cell.

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A portable chest roentgenogram was reported to reveal pneumonitis in the left lower lung field.

Hospital Course.—Gastric aspiration by Levine tube produced 1,000 c.c. of tan-colored fluid; catheterization produced 300 c.c. grossly normal urine. About two hours after admission the appearance of cervical subcutaneous emphysema was noted. Chest roentgenograms taken about 7:00 P.M. revealed evidence of left pleural effusion with blunting of the right costophrenic angle. Left thoracentesis produced dark brown, turbid, watery fluid resembling old hemolyzed blood. No significant odor was noted. Testing with Toepfer's reagent revealed no free acid in the aspirated fluid. The diagnosis of spontaneous rupture of the esophagus was made and the patient transferred to the Thoracic Surgical section. Open exploratory thoracotomy was considered but discarded because of the fear of serious hemorrhage due to the hemorrhagic disorder. Continuous gastric suction by indwelling Levine

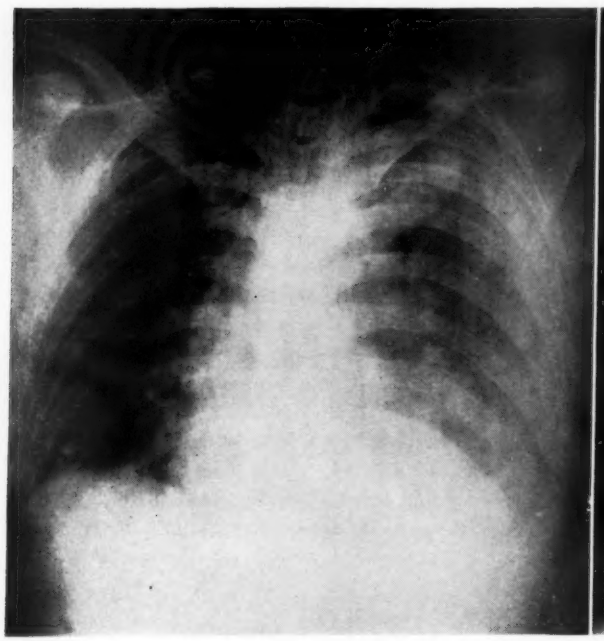

Fig. 1.

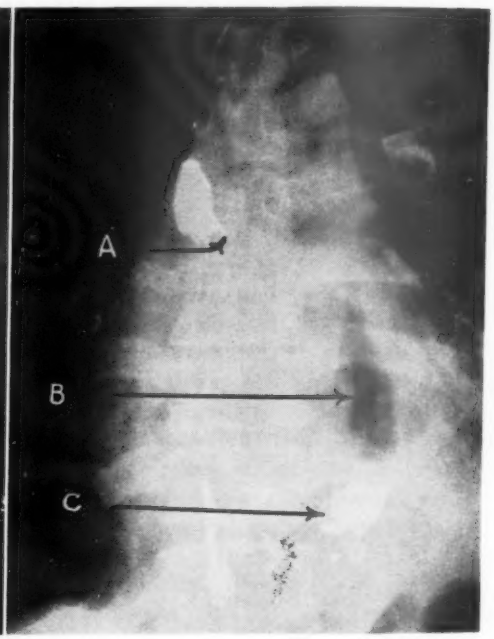

Fig. 2.

Fig. 1.—Admission roentgenogram (portable).

Fig. 2.—Roentgenogram following Lipiodol swallow. *A*, Out-pouching of diverticulum in midportion of esophagus. *B*, Retrocardiac air and fluid collection. *C*, Lipiodol escaped into posterior mediastinum.

tube was instituted. A No. 24 Foley catheter was inserted through the left seventh intercostal space in the midaxillary line by trocar and cannula and connected to underwater seal drain. About 500 c.c. of the dark brown, turbid fluid were evacuated. Oxygen was administered by nasal catheter. Penicillin, 200,000 units every six hours, and streptomycin, 1 Gm. daily, with appropriate intravenous fluids were given. Morphine was only partially effective in control of pain, the patient continuing to moan at frequent intervals during the first twenty-four hours. Rectal temperature rose to 104° F. the night of admission and did not fall to normal for several days. Sixteen hours after admission the blood pressure had dropped to 50/0. The pulse was feeble but regular at 100 per minute, the skin was warm and dry, and the superficial veins appeared mildly distended. The patient responded poorly to questions, appearing too ill to bother. During the second hospital day the blood pressure rose to 70/50, the pulse became better in quality, and the patient appeared improved. By the third day, blood pressure was stabilized at about 120/80, drainage through the thoracotomy tube

was minimal, the subcutaneous emphysema was clearing, and urinary output was adequate with parenteral fluids. Nasal oxygen was discontinued. On the fourth day gastric suction was discontinued. Physical and roentgenologic examinations revealed evidence of atelectasis of the left lung, which cleared readily after tracheal catheter suction. The intercostal catheter was removed on the fifth day, as there was no drainage and the lung was well expanded. General improvement continued until the seventh hospital day when a precordial friction rub was noted. Increased amounts of intrapleural fluid and air were noted on the roentgenogram.

Thoracentesis produced 200 c.c. of thin, muddy-colored, turbid, foul-smelling fluid. Oral intake of food and fluid had been denied throughout; nutrition was maintained by parenteral glucose-protein hydrolysate solution and vitamins in hopeful anticipation of natural healing of the rupture. Increase in the empyema and intrapleural air indicated persistence of the rupture. On the ninth hospital day a roentgenogram made following a swallow of iodized oil apparently revealed the site of esophageal rupture to be just below the left main bronchus. Collections of air, fluid, and oil were noted in the posterior mediastinum as well. A short segment of the eighth rib was resected and the empyema drained with a large rubber tube connected to an underwater seal. The following day a Levine tube was passed into the stomach and tube feeding begun. Transfusions of whole blood were used to correct the secondary anemia.

Some of the feedings appeared in the thoracotomy drainage fluid. Gradually hepatic enlargement, dependent edema, and distention of superficial veins appeared. The precordial friction rub persisted. Fluoroscopy revealed progressive cardiac enlargement with diminished pulsations. Electrocardiogram tracings were consistent with pericardial inflammation. Salt was removed from the diet and diuretics were given intravenously with little reduction in the edema. On the eleventh day, pericardial aspiration produced 20 c.c. of blood-tinged fluid. Repetition on the thirteenth day produced 200 c.c. of grossly bloody fluid which ran slowly from the needle but could not be aspirated. Eighty c.c. of air were injected into the pericardial space. Fluoroscopy now revealed marked thickening of the pericardium with loculation of air, but no fluid level was seen. Slight clinical improvement followed. Finally, on the fourteenth day, the absolute necessity for alleviation of the cardiac tamponade became apparent. Constant loss of food through the esophagus into the chest when injected into the stomach by tube made this method of feeding unacceptable. Leaking of the feedings contributed to the mediastinal and pleural infection. The thoracotomy tube was located too high for adequate dependent drainage of the empyema.

Two surgical teams were utilized. Incisions were made over the right fourth rib anteriorly and in the left upper abdomen. The pleural space was entered through the bed of the resected fourth rib. The pericardium was found to be markedly distended, edematous, somewhat ecchymotic, and from 10 to 15 mm. in thickness. A large segment of the pericardium was excised anterior to the phrenic nerve. The pericardial space was filled with old hemolyzed bloody fluid and masses of fibrin appearing not unlike a clotted hemothorax. This was evacuated. The chest was closed after an intercostal Foley catheter was placed for underwater seal drainage. Following cardiac decompression, the pulse pressure increased 30 mm. Hg. Blood pressure preoperatively was 70/55. At the conclusion of the procedure, it was 120/74. Concurrently a Witzel-type catheter jejunostomy was done by the other surgical team.*

The foregoing procedures were completed with the patient in the supine position. He was then turned to the right lateral position, and drainage of the empyema space through the bed of the resected eleventh rib was done. The upper drainage tube was removed and the wound closed with loosely placed sutures.

Surprisingly, the hemorrhagic disorder added no apparent difficulty to the procedures which required a total of one hour and twenty-five minutes.

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Postoperatively there was rapid clearing of edema, venous distention, and hepatic enlargement. Jejunostomy feedings were begun on the second postoperative day and the right-sided intercostal drainage tube removed on the third day. Fever subsided on the fourth postoperative day. On the eighth postoperative day, roentgenograms made during barium swallow revealed a diverticulum located in the area thought to be the site of rupture. No leakage of barium from the esophagus was seen in this area but barium was noted subsequently in the posterior lower mediastinum. Some of the barium appeared in the thoracotomy drainage tube, as did methylene blue solution taken orally. At this time, rupture of the esophageal diverticulum due to coughing was thought to be the cause of the esophagopleural fistula. Cautiously the patient was allowed to swallow increasing amounts of liquids, some of which continued to appear in the thoracotomy drainage. Jejunostomy feedings were discontinued on the twenty-ninth postoperative day, as the patient could now tolerate orally a diet of the convalescent peptic ulcer type. Jejunostomy tube was removed on the thirty-second postoperative day. Loss of ingested food and fluid through the thoracotomy tube gradually ceased. The subsequent recovery was uneventful, and the empyema healed within two months of admission.

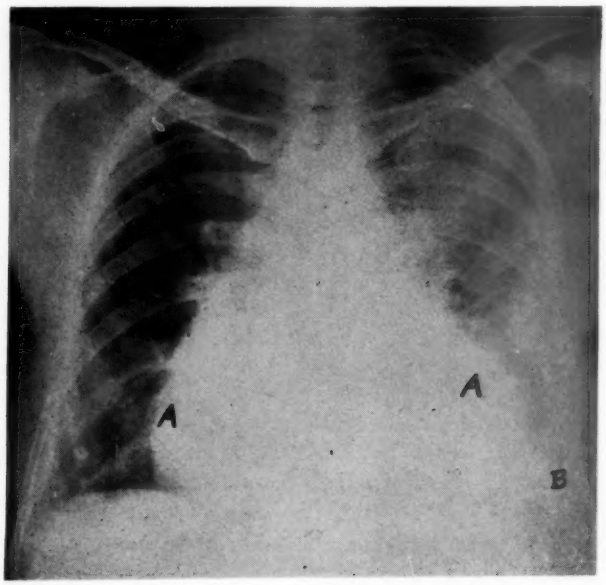

Fig. 3.—Roentgenogram before partial pericardiectomy. *A*, Marked enlargement of cardiac shadow. *B*, Minimal collection of intrapleural fluid, left.

During a follow-up barium study on March 24, 1951, a deformity of the lower esophagus was noted. Comparison with the earlier films revealed this deformity to be the site of esophageal rupture, and the esophageal diverticulum to be a matter of coincidence. Natural healing of the esophagopleural fistula occurred with resultant deformity as noted on the last esophagram.

He had no dysphagia nor other complaint.

Follow-up examination on March 24, 1951, found the patient in continued excellent health.

Comment.—So-called spontaneous rupture of the apparently normal esophagus has been the subject of excellent reviews presenting the historical aspects in interesting detail.[1, 5, 6, 10] The characteristic features leading to the correct diagnosis, and the requisites for successful therapy of this clinical entity have

been emphasized.[1, 10, 11] Further elaboration here of the clinical features, physical and roentgenographic findings, and other aids in the diagnosis of rupture of the apparently normal esophagus would be superfluous.

This case report demonstrates the fallacy and danger of conservative measures in the treatment of the accident. The presence of a hemorrhagic disorder in this patient was the principal reason not only for the delay in diagnosis after admission to the hospital but also for withholding early definitive operative treatment once the diagnosis had been established. Effective evacuation of the intrapleural fluid and expansion of the underlying lung were provided by intercostal catheter drainage. However, adequate decompression of the mediastinum was not effected by the intrapleural drainage. This was demonstrated by the severe hypotension associated with superficial venous distention, warm dry skin, and a moderately rapid pulse rate during the early hospital course. Later the irritation of continued esophageal leakage probably caused the pericardial effusion. It is believed that the bloody character of the fluid resulted from the

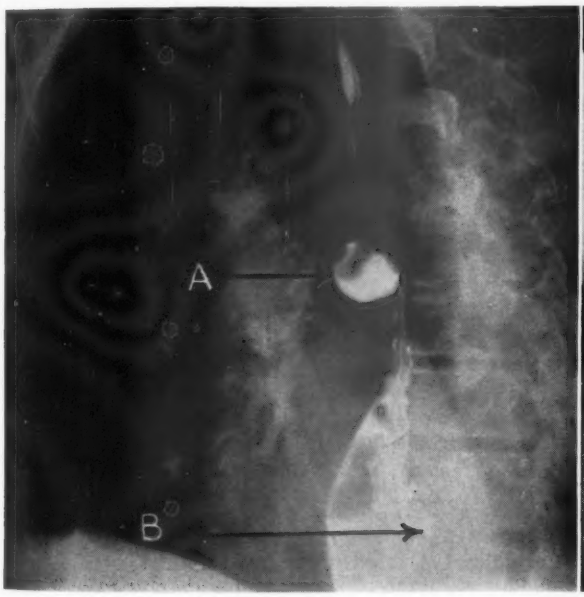

Fig. 4.

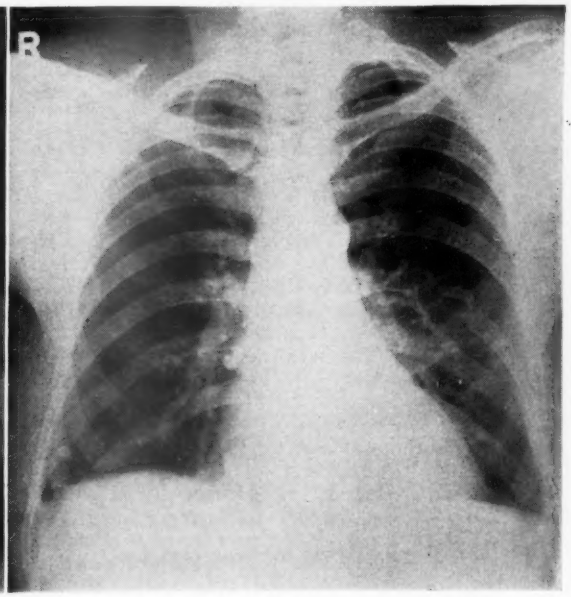

Fig. 5.

Fig. 4.—Roentgenogram three and one-half months after accident. Left anterior oblique view revealing *A*, Diverticulum in midportion. *B*, Deformity about diaphragm at location of rupture.

Fig. 5.—Roentgenogram three and one-half months after accident.

patient's blood dyscrasia. Whether or not the blood dyscrasia contributed to the delay in spontaneous closure of the esophageal rent is conjectural. Esophageal leakage persisted in spite of the fact that all oral foods and liquids were withheld during the first week of treatment. Later, use of the Levine tube for feeding was also ineffective in preventing esophageal leakage. This fact should not detract from the recognized value of continuous gastric suction in the early supportive treatment.

In retrospect, the smooth course of this patient during and following the desperate operative measures suggests that early open thoracotomy, adequate mediastinal drainage, and suture of the esophageal tear might have been followed by a rapid uncomplicated recovery. The important assistance given by the use of large doses of the antibiotics should not be overlooked.

This case is of interest in two other respects. It is the only one reported, to our knowledge, due to severe coughing. It is also the only instance of the accident in which a coincidental esophageal diverticulum has been noted.

SUMMARY

1. A case of rupture of an apparently normal esophagus due to coughing is reported.

2. Recovery was hindered by the pre-existing blood dyscrasia to the extent that there was delay in diagnosis, inadequate early therapy, and the later appearance of cardiac tamponade.

3. Closed drainage, rib resection drainage, partial pericardiectomy, and jejunostomy were performed before recovery was assured.

4. A diverticulum of the mid-thoracic esophagus was a coincidental finding.

REFERENCES

1. Barrett, N. R.: Spontaneous Perforation of the Esophagus. Review of the Literature and Report of Three New Cases, Thorax **1**: 48-70, 1946.
2. Barrett, N. R.: Report of a Case of Spontaneous Perforation of the Esophagus Successfully Treated by Operation, Brit. J. Surg. **35**: 216-218, 1947.
3. Cliffton, E. E.: Spontaneous Rupture of the Esophagus. Report of Two Cases: One With Recovery After Surgical Repair, Ann. Surg. **130**: 1066, 1949.
4. Dunavant, D., and Skinner, E. F.: Spontaneous Rupture of the Esophagus, SURGERY **29**: 527, 1951.
5. Fitz, R. H.: Rupture of the Healthy Oesophagus, Am. J. Med. Sc. **73**: 17-36, 1877.
6. Flipse, M. E.: Spontaneous Rupture of the Esophagus, Dis. Chest **19**: 165-189, 1951.
7. Frink, N. W.: Spontaneous Rupture of the Esophagus; Report of Case With Recovery, J. Thoracic Surg. **16**: 291-297, 1947.
8. Gardner, C. M.: "Spontaneous" Rupture of the Esophagus, Arch. Surg. **59**: 710-712, 1949.
9. Graham, E. A.: The 1943 Yearbook of General Surgery, Chicago, 1944, Year Book Publishers.
10. Kinsella, T. J., Morse, R. W., and Hertzog, A. J.: Spontaneous Rupture of the Esophagus, J. Thoracic Surg. **17**: 613-631, 1948.
11. Lynch, J. P.: Spontaneous Perforation of the Esophagus; Report of Three Cases Successfully Treated Surgically, New England J. Med. **241**: 395-400, 1949.
12. Moore, J. A., and Murphy, J. D.: Spontaneous Rupture of the Esophagus; Report of One Case, With Recovery, J. Thoracic Surg. **17**: 632-638, 1948.
13. Olsen, A. M., and Clagett, O. T.: Spontaneous Rupture of the Esophagus; Report of a Case With Immediate Diagnosis and Successful Surgical Repair, Postgrad. Med. **2**: 417-421, 1947.
14. Overholt, R.: Cited by Flipse.
15. Scholefield, J.: Spontaneous Perforation of the Esophagus, Surgical Repair With Recovery, Brit. M. J. **1**: 348, 1949.

SIMULTANEOUS BILATERAL RADICAL NECK DISSECTION WITH RECOVERY

Report of Two Cases

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THE operation of unilateral radical neck dissection is a well-established surgical procedure. Its benefits are so well recognized that the minimal morbidity and mortality resulting from the operation are accepted as reasonable risks. The same is not true for bilateral radical neck dissection performed in two stages. In the latter the mortality is reported to be much higher than for the unilateral operation. Duffy[1] stated that the mortality from bilateral neck dissection would most likely exceed the number of cases cured by this procedure. Brown and McDowell[2] report one death from a subdural hemorrhage among the cases in which they performed the staged bilateral procedure. They felt that the mortality was due to a considerably raised intracerebral venous pressure. Of two cases, Sandberg[3] reports one death. Modlin[6] records six and Gius and Grier[5] report eight cases with no surgical mortality. In our nine cases, one patient died two hours after surgery without regaining consciousness and with the cause of death undetermined at autopsy. Indeed, most of the reports on the mortality of staged bilateral neck dissections are based on presumption rather than on facts. We, therefore, feel that Martin's[4] report of thirty-four cases with no mortality establishes the two-stage bilateral neck dissection as a safe procedure.

The morbidity of the two-stage bilateral procedure is definitely worthy of consideration. These patients almost invariably and immediately have marked edema and cyanosis of the face. The cyanosis usually disappears in twenty-four hours, whereas the edema may even increase for a few days, particularly on the side of the second procedure. After about seven to ten days the edema disappears from the upper half of the face but may persist for months and sometimes permanently about the lower half of the face, particularly along the inferior mandibular margin. We have not personally observed any psychotic changes or disorientation directly attributable to the operation. No reports of eyeground changes or increased disabling intracranial pressure have been recorded.

The fact that all reported cases of bilateral radical neck dissection have been two-stage procedures indicates the apprehension existing regarding the safety of simultaneous bilateral radical neck dissection. The unknown factor has been with respect to the minimal interval which may be allowed to elapse before the second neck dissection can be done safely. Here again, there is a great divergence of opinion based primarily on impression. Brown and McDowell[2] wait several months and Jorstad and Verda[7] suggest an interval of four

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to six months which, they rightfully believe, would make the case inoperable if the involved nodes were bilaterally present on entrance. Martin[4] has performed a second side neck dissection six days after the first, but prefers to wait three weeks. We have allowed at least three weeks to elapse before performing the second side neck dissection. This period has frequently been observed to be a safe one. Following such an interval, the patient's general condition and the local health of the tissues, as determined by healing and loss of inflammatory reaction and edema, are usually in a satisfactory preoperative state. It is felt that a three-week delay will not jeopardize whatever chances the patient may have for recovery. In part, this interval is based on empiricism, for a shorter period, may, if tried, prove just as satisfactory.

HISTORICAL REVIEW

The constantly shrinking interval which we have observed and experienced as being safe has suggested to us the possible feasibility of a simultaneous bilateral radical neck dissection. Such a procedure would entail the one-stage excision of both internal, both external, and both anterior jugular veins from the level of the mandible to the clavicle, and of the main superficial and deep lymphatic chains of both anterior and both posterior triangles of the neck en masse. A review of the literature revealed frequent mention of this possibility but no recorded cases were found. In 1900, Ewald[8] reported a case of wide intraoral excision combined with a limited bilateral upper neck dissection in which only about 3 cm. of each of the upper ends of the internal jugular veins were excised. This patient died in one hour without regaining consciousness. Dangel,[9] in 1905, performed a similar intraoral and bilateral upper neck dissection in which he excised not over 4 cm. of the upper portions of both internal jugular veins. His patient recovered. He manifested facial cyanosis for only about ten minutes. In neither case did the surgical procedure involve more than a limited bilateral upper neck dissection with excision of only a small section of the internal jugular veins. Gius[5, 11] who has reported excellently the venous adaptation following the two-stage bilateral radical neck dissection was not aware of any reports of bilateral simultaneous excision of the internal jugular veins. The series of cases reported and reviewed by Evans[10] are not comparable, as these were instances of simple ligation of the upper ends of the internal jugular veins in one or two stages.

ANATOMY

Anatomically, the successful consummation of simultaneous bilateral radical neck dissection is dependent upon the efficacy of the vertebral system of veins to take over immediately and adequately the venous drainage from the brain, intracranial and extracranial tissues, and the anterior and lateral aspects of the neck. This system of vertebral veins, so well described by Batson[12-14] and Gius,[5, 11] passes as a plexiform network, primarily in a longitudinal direction, both intraspinally between the dura and the vertebrae and extraspinally between the vertebrae and the erector spinae group of muscles. Cephalad the system communicates through the foramen magnum with the occipital and

basilar sinuses which connect with the major intracranial dural sinuses. In addition there are numerous basal skull emissary veins which communicate with this system. At all vertebral levels the longitudinal vertebral system of veins anastomose transversely with each other and with the intercostal and lumbar veins which connect, either directly or by way of the azygos system, with the caval veins. This vertebral-azygos-caval route provides a detour of venous return from the brain to the right heart. Usually, the vertebral system of veins is constantly functioning and, due to a lack of valves and low venous pressure, the blood may travel in either direction. Under abnormal conditions of obstruction to the superior caval veins,[12] the vertebral system has clinically demonstrated its capability of increasing its carrying capacity. Under the circumstances of a one-sided radical neck dissection this is probably not an important factor but when the opposite jugular system is removed the return load is primarily shunted to the vertebral system. It was to allow for a compensatory increase in the cross-sectional caliber of the vertebral system of veins that an interval of several weeks, at least, was established between the two stages of a bilateral radical neck dissection. Clinically, the question had not yet been answered as to whether or not the vertebral system of veins would be adequate to the task of increased venous drainage imposed upon it by the simultaneous bilateral removal of the internal, external, and anterior jugular veins and their immediate tributaries, between the mandible and clavicle, as would be the case in a one-stage bilateral radical neck dissection. Because of the ligation of the anterior facial vein in this operation, the return of venous blood from the intracranial structures by way of the by-pass of the cavernous sinus and ophthalmic vein is blocked. In addition, the pterygoid and pharyngeal plexus, the superior and middle thyroid veins, the transverse cervical veins, and the common facial veins with their posterior facial and occipital anastomoses would be blocked off from the jugular system. Under such conditions the only superior caval veins assisting the vertebral system would be the inferior thyroid, deep cervical, and vertebral veins of the subclavian and innominate veins, and possibly the transverse scapular veins by way of the shoulder area and posterior neck regions.

CASE HISTORIES

In the two cases here recorded the vertebral system of veins with limited superior vena caval assistance was found to be adequate to maintain the venous drainage from the brain, and from the intra- and extracranial and neck tissues, following simultaneous bilateral radical neck dissection.

CASE 1.—J. B., a 65-year-old man, first saw his physician in June, 1948, for hoarseness which began in January, 1948. At the time, clinically involved and enlarged neck nodes were present bilaterally in both upper jugular areas. He received a full course of x-irradiation through two ports placed over the neck nodes crossfiring the larynx. Due to glottic obstruction, an emergency tracheostomy was performed in June, 1948. Both the primary lesion and the metastatically involved upper neck nodes regressed very little. In September, 1948, there was still present an ulcerated carcinoma involving the base of the epiglottis, valleculae, pre-epiglottic space, and base of the tongue. The upper jugular nodes were firm and enlarged, especially on the left. The tracheostomy tube was still in place. The patient was

weak and anemic and suffering great pain and discomfort. The breath was foul and there was a purulent discharge from the tracheostomy stoma and mouth. In June, 1949, the patient was scheduled for a laryngoglossectomy and a left radical neck dissection. Upon the successful completion of this procedure, it was decided to explore the residual, but smaller, right upper neck mass. While so doing, a large rent was made in the infiltrated right internal jugular vein. The vessel was cleared and ligated above the level of the posterior belly of the digastric muscle. The immediate reaction to the ligation of the second internal jugular vein was a decrease in the blood pressure from 140/70 to 80/50. Subsequently, the blood pressure rose steadily during the next hour to a level of 210/100. The pulse did not vary significantly, but the respiratory rate fell from 24 to 14 per minute. A right radical neck dissection was then consummated with removal of the right internal, external, and anterior jugular veins. About one hour after the ligation of the second internal jugular vein, the

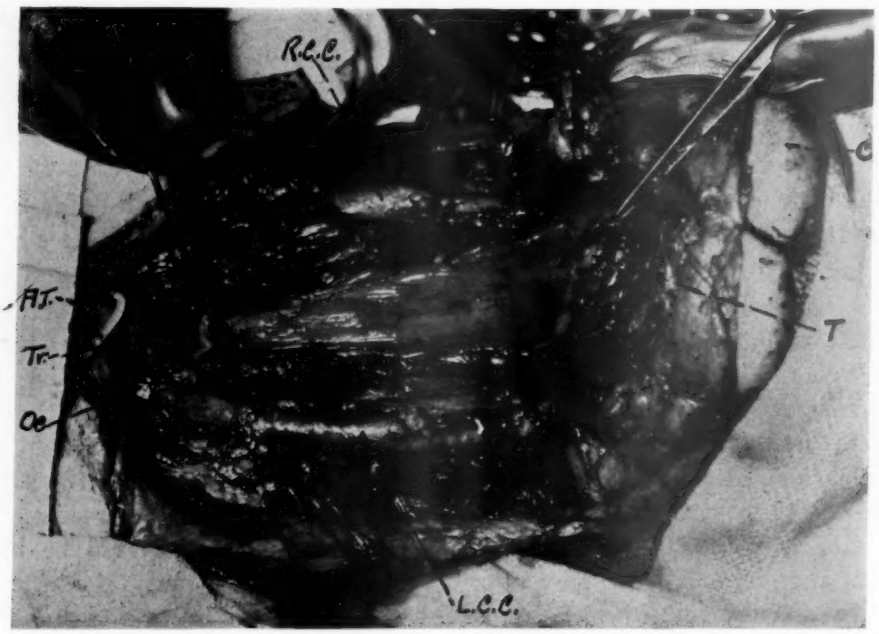


Fig. 1 (Case 1).—The surgical field after removal of the larynx, thyroid, strap muscles, hyoid bone, base of tongue, combined with a bilateral radical neck dissection. The common carotid arteries (*R.C.C.* and *L.C.C.*), posterior esophageal and hypopharyngeal walls, lower esophageal stoma (*Oe*), lower tracheal stoma (*Tr*), base of tongue (*T*), anesthetic tube below the permanent tracheal stoma (*A.T.*), and the chin (*C*) are visualized.

anesthetist stated that the blood pressure and respirations were returning to normal. During this period, no additional anesthesia was given. Apparently the passive hyperemia maintained a more prolonged contact of the anesthetic drugs with the cerebrum due to the marked retardation of the venous return. Following this one-hour period, the patient's condition returned to what it was prior to the ligation of the second internal jugular vein. Marked cyanosis and edema of the face were immediately noted. The cyanosis cleared after twenty-four hours. The edema began to recede at the end of the first postoperative day and cleared rather rapidly during the first two weeks. It did not seem as if the cyanosis and edema in this case were more pronounced than those which had been noted in some cases of which we had previous clinical observation where a second radical neck dissection was performed within three to six weeks after the first. By the twelfth postoperative week all of the edema had disappeared except in the soft tissues overlying the mandible. He died of metastatic mediastinal disease in December, 1949. Autopsy revealed no unusual cerebral or intracranial alterations which could be accounted for on the basis of the extensive vein excisions.

CASE 2.—R. L., a 56-year-old man, complained of a sore throat in the fall of 1947. Tonsillectomy in January, 1948, and again in May, 1948, gave no relief. A tumor was excised from the left neck in May, 1950, and revealed metastatic cancer. Following this, a primary epidermoid carcinoma was found in the larynx. Tracheostomy was followed by deep x-ray therapy in July, 1950, without relief. Subsequently palliative therapy failed to relieve him. When seen in November, 1950, there was a fungating cancer of the skin of the left anterior triangle of the neck, 8 cm. in diameter, at the site of the previous incisional biopsy. There

Fig. 2.

Fig. 3.

Fig. 2 (Case 1).—*A*, Preoperative. *B*, Postoperative, two months, showing residual mandibular edema.

Fig. 3 (Case 1).—*A*, Postoperative, one week, showing marked edema of face. *B*, Postoperative, two months, showing marked regression of edema.

were firm, enlarged, metastatically involved nodes in both submaxillary, and upper and middle jugular areas. The primary carcinoma involved the entire epiglottis, left hemilarynx, and pyriform sinus, and extended into the left base of the tongue.

On Dec. 20, 1950, under intratracheal nitrous oxide-oxygen and Pentothal sodium anesthesia he underwent a combined bilateral radical neck dissection with a laryngoglossectomy, partial pharyngectomy, wide excision of the fungating cancer of the skin of the left neck with split-skin graft repair and pharyngostome. During the entire procedure spinal manometer readings were taken. The readings, because of the setup, are given in relative units rather than absolute millimeters of pressure. The preligation reading was 600 units. Twenty minutes after the start of the operation the reading was 560 when the lower end of the left internal jugular vein was ligated. During the next twenty minutes it rose to 650 and then dropped rapidly to 400 in thirty minutes. At this point the second (right) internal jugular vein was ligated and the spinal manometer reading rose rapidly to 900 in twenty minutes. In ten minutes it dropped to 750 at which point the upper end of the second (right) internal jugular vein was ligated. The pressure over the next eighty minutes dropped slowly to 600 where it remained with very little variation until the end of the operation.

Fig. 4 (Case 2).—Preoperative, showing fungating biopsy site of left side of neck, 8 cm. in diameter.

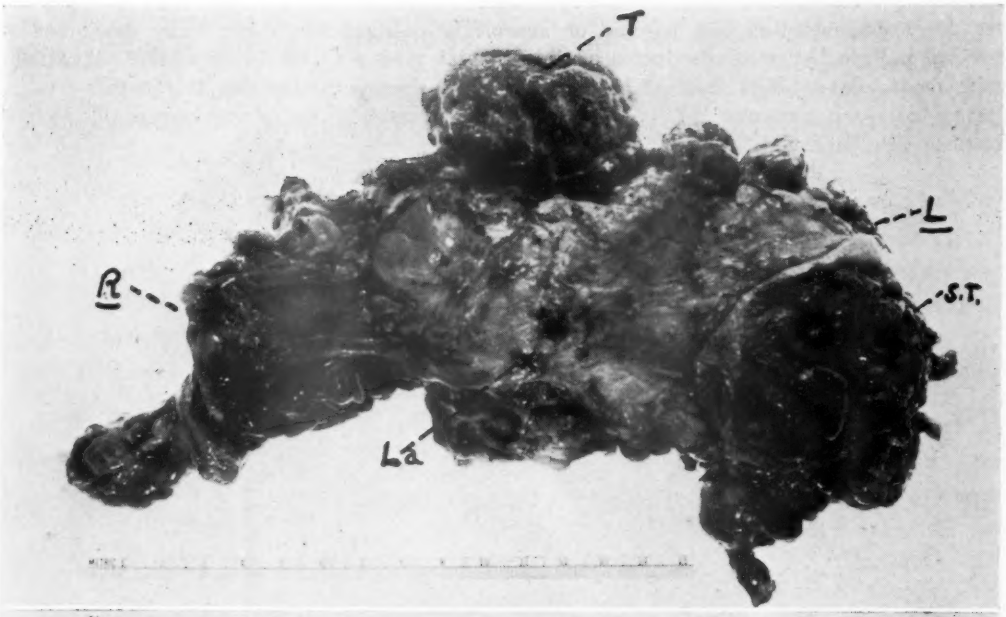
Preoperatively the blood pressure was 100/70. After the ligation of the first (left) internal jugular vein it dropped to 85/60 at which point the lower end of the second (right) internal jugular vein was ligated. Following this the pressure rose to 125/85 in thirty minutes, after which it dropped to 110/70, and then rose to 125/70 at the termination of the operation.

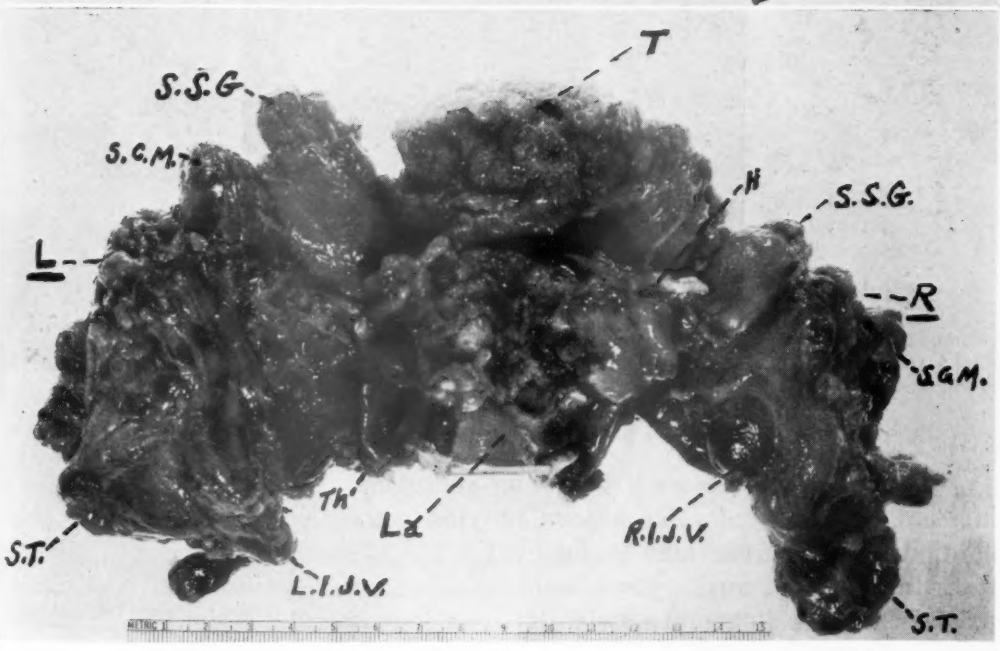
The pulse rate dropped from 85 to 60 with the first ligation, but rose in thirty minutes to 75. At this point the second ligation was performed, causing the pulse to drop to 65. It rose again to 75 in thirty minutes, but later dropped to between 60 and 70 where it remained until the end of the surgery.

The respiratory rate, 16 preoperatively, was unchanged with the ligation of the first (left) internal jugular vein, but rose to 22 when the second (right) was ligated, and remained between 22 and 26 for almost two hours, when it rapidly dropped to between 12 and 14 where it remained until the end of the operation.

During the surgical period of five and one-half hours, 3,500 c.c. of blood were transfused. The patient developed cyanosis, which disappeared in twenty-four hours, and very

A.





B.

Fig. 5 (Case 2).—*A*, Anterior view: larynx (*La*) pre-epiglottic space, base of the tongue (*T*), and fungating site of the skin (*ST*), the tissues of the right (*R*) and left (*L*) neck dissections as removed in continuity with the larynx and base of the tongue. *B*, Posterior view: surgical specimen of the block excision of the simultaneous dissection of the right (*R*) and left (*L*) neck in combination with the larynx (*La*). *L.I.J.V.* is left internal jugular vein; *R.I.J.V.*, right internal jugular vein; *S.T.*, supraclavicular triangle; *S.C.M.*, sternocleidomastoid muscle; *S.S.G.*, submaxillary salivary gland; *H.*, hyoid bone; *T*, base of tongue; and *Th*, left lobe of thyroid.

marked facial edema which is still (three months postoperatively) extensive about the mandible. There is, as yet, no evidence of recurrence. He is tube fed through his pharyngostome and has gained about twenty-five pounds. He has always been well oriented and has never demonstrated any psychic or neurologic changes which might be attributed to cerebral passive hyperemia or increased intracranial pressure. He is up and about without pain, feeds himself, does most of his dressings, and smokes through his tracheostomy stoma during his spare moments. If, in due time, there is no evidence of recurrence, his pharyngostome will be closed.

Fig. 6 (Case 2).—Postoperative, three months, with marked residual edema of the mandibular area and pharyngostome.

DISCUSSION

In view of the recovery following simultaneous bilateral removal of the internal, external, and anterior jugular veins in these two cases, it is quite possible that similar success may be obtained in other instances where this operative procedure is indicated. Such indications are the presence of controllable primary midline intraoral or visceral neck lesions and concomitant bilaterally involved cervical lymph nodes. Such primary lesions are frequently found in the larynx, cervical esophagus, thyroid and mouth. In the latter group, malignant lesions of the lip, tongue, and floor of the mouth are most frequently associated with bilateral cervical lymph node involvement, especially if the lesion is close to, or crosses, the midline. Previously, cases of this type were managed surgically by operating in stages. First, the primary lesion was removed alone, or in conjunction with a one-sided radical neck dissection. This was followed in ten to twenty days by the radical neck dissection of the other side. Such

staging frequently would entail cutting through tumor or into involved lymphatic channels, resulting in a growth of residual carcinoma from these transected areas into the operative field. This often takes on the characteristic appearance of a lavalike growth of cancer so intimately involving the periphery of the already cleared operative field that its subsequent clean removal cannot be accomplished. A simultaneous bilateral radical neck dissection carried out in such cases would tend to eliminate these complications.

Surgery of this extent is not for palliation. Chances for cure must be presumed to be enhanced before a one-stage radical bilateral neck dissection is undertaken. There is no indication for such an operation if neck dissection is elective, since the operation in stages would be expected to give less mortality and a shorter morbidity.

SUMMARY

Two surgically successful cases of simultaneous bilateral radical neck dissection are reported. The en masse procedure included laryngectomy with removal of the hyoid bone, the base of the tongue, the pre-epiglottic area, and the strap muscles, and the excision bilaterally of the anterior, external, and internal jugular veins.

REFERENCES

1. Duffy, J.: In Pack, G. T., and Livingston, E. M.: Treatment of Cancer and Allied Diseases, Vol. I, New York, 1940, Paul B. Hoeber, Inc., p. 581.
2. Brown, B., and McDowell, F.: Neck Dissections for Metastatic Carcinoma, Surg., Gynec. & Obst. **79:** 115-124, 1944.
3. Sandberg, I. R.: Dissection of the Cervical Lymph Node Regions for Metastasis From Malignant Tumors of the Lip, Oral Cavity and Pharynx, Acta chir. scandinav. **92:** 99, 1945.
4. Martin, Hayes E.: Personal communication.
5. Gius, J. A., and Grier, D. H.: Venous Adaptation Following Bilateral Radical Neck Dissection With Excision of the Jugular Veins, SURGERY **28:** 305-321, 1950.
6. Modlin, J.: In discussion of Gius.[5]
7. Jorstad, L. H., and Verda, D. J.: Cancer of Tongue; Its Diagnosis and Treatment, S. Clin. North America **24:** 1077-1088, 1944.
8. Ewald, C.: Tod unter vasomotorishen störungen nach resection beider venae jugulares internal, Wein. klin. Rundschau. **14:** 673, 1900.
9. Dangel, M.: Ueber die unterbindung den vena jugularis interna. (Ein fall von doppelseitiger unterbindung), Beitr. z. klin. Chir. **46:** 495, 1905.
10. Evans, M. G.: Bilateral Jugular Ligation Following Bilateral Suppurative Mastoiditis, Ann. Otol. Rhin. & Laryng. **51:** 615-625, 1942.
11. Gius, J. A.: Personal communication.
12. Batson, O. V.: Anatomical Problems Concerned in the Study of Cerebral Blood Flow, Federation Proc. **3:** 139-144, 1944.
13. Batson, O. V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastases, Ann. Surg. **112:** 138-148, 1940.
14. Batson, O. V.: The Role of the Vertebral Veins in Metastatic Processes, Ann. Int. Med. **16:** 38-45, 1942.
15. Gius, J. A.: Some Observations on Vascular Adjustments Following Interruption of Major Venous Channels, West. J. Surg. **57:** 453-462, 1949.

DISCUSSION

DR. O. V. BATSON, Philadelphia.—In the extensive dissection described by Dr. Perzik, some of the connections from the neck to the vertebral veins have been removed. Tissue edema following surgery appears to be associated with venous ligation accompanied by lymphatic ligation.

Perhaps the mandible and particularly the chin is the head-part most remote from the vertebral plexus of veins. The lymphatic drainage from the mandible has been removed, and

the venous drainage from the mandible would have the longest route to follow before attaining the plexiform network of the vertebral veins. Further, in the sitting posture, the chin is lower than its new venous outflow.

Patients accustomed to occupations in which holding the breath is exaggerated should be much better risks for bilateral venous ligation than patients less accustomed to straining. That is, freight handlers, miners, and painters should make good patients.

Cases of effort thrombosis are multiplying in the literature. I have had the opportunity to study four cases. Three had a total occlusion of the superior vena cava, and one of these three had, in addition, thrombosis of the vena azygos major. In these cases, not only the blood from the head and neck, as in the radical dissection cases, must return by way of the vertebrals, but in addition all the blood from both upper extremities.

Variations in blood pressure, pulse, and respiratory rates do not seem too unusual when one recalls the sympathetic nerve plexus about the great vessels in the neck. When the surgeon lays bare the vessels for ligation, he has performed a Leriche operation on that vessel, for the plexus runs in the tunica adventitia.

There is clinical precedence for the bilateral ligation of the internal jugular veins. When mastoiditis was a problem, bilateral ligation of the internal jugular veins was sometimes done. Ligation of the external jugular veins is ordinarily an unrecorded procedure in ligation of the internal jugular veins. True, the anterior jugulars would not be ligated, but their small size and irregular anatomy makes them relatively insignificant in the major problem of drainage.

Support to the cardiovascular system during the operation and in the postoperative period should be routine, to insure an adequate minute volume flow of blood to the brain.

DR. J. ARMES GIUS, Portland, Ore.—The point that bilateral simultaneous radical neck dissection is feasible is supported by these cases. However, I would personally be hesitant to apply such treatment because of the hazard of complete venous decompensation. It is granted that an occasional situation would call for this procedure if one is to be consistent in the application of the fundamental rule of cancer surgery, that one should "never cross a cancer field."

It is well known that cancer of the lip, tongue, oral cavity, nasopharynx, sinuses, etc. are fatal largely because of their local and cervical effects on nutrition, respiration, and circulation. Distant spread is uncommonly a consideration. Cancer can be surgically attacked in the neck with a respectable salvage rate. It is therefore consistent with our aim in surgical treatment of cancer elsewhere to attempt to extend operation in head and neck cancer where it may conceivably contribute to an increased cure rate.

DR. TRACY J. PUTNAM, Beverly Hills, Calif.—Dr. Perzik has given us unquestionable proof that it is possible to excise both internal jugular veins simultaneously, without serious embarrassment of the cerebral circulation. This is an important feat in itself, and an illustration of the fact that many procedures which have been avoided on theoretical grounds are actually feasible and advantageous. Perhaps we should even have been able to predict a successful outcome of such an operation. It is well known that there is an enormous excess capacity in the venous system, and the venous collaterals from the cranial cavity, such as the mastoid emissaries and vertebral veins can transmit large amounts of blood, as neurosurgeons know to their sorrow. There is an ample collateral venous circulation within the skull, so that the location of the outflow does not seem to be of great importance.

An excess of carbon dioxide in the cerebral circulation leads to a vasodilatation, and consequently, a considerably increased volume flow. There are no disturbances of consciousness with increases of carbon dioxide content up to 10 or 15 volumes per cent. Much higher concentrations—up to 30 volumes per cent—may be tolerated for minutes at a time, although some damage to the white matter may occur with a long-continued passive congestion of extreme degree. Clearly, such complications have not yet been encountered.

TANTALUM MESH REPAIR OF HERNIATION OF BLADDER FOLLOWING RETROPUBIC PROSTATECTOMY

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TANTALUM mesh has been widely used for the repair of defects in the abdominal wall since its introduction in 1947.[1] Lacking knowledge as to the effect of prolonged contact of this material upon peritoneal surfaces, or upon intra-abdominal viscera, there was at first some hesitancy in using the mesh when peritoneum or other tissue could not be interposed between it and the abdominal contents. Recent experimental work and successful clinical use by Koontz indicate that tantalum mesh may be safely used in direct contact with intestinal surfaces.[2, 3] The following case illustrates the use of tantalum mesh in direct contact with the urinary bladder.

CASE REPORT

F. M., a white man 48 years of age, was admitted to The Johns Hopkins Hospital on Feb. 28, 1951, complaining of perineal pain of three years' duration. Eighteen months previously, he had undergone retropubic prostatectomy elsewhere without relief of symptoms. This operation was, however, followed by an incisional hernia. Two subsequent attempts at repair had been unsuccessful.

The admission examination revealed general physical findings within normal limits. There was a low midline incision scar. A large, but reducible, hernia presented just above the symphysis pubis, through a defect 10 cm. in diameter. There was a marked tenderness of the left seminal vesicle on rectal examination. On March 2, 1951, the lower midline incision was reopened and the infected left seminal vesicle removed. The incisional hernia was repaired by bringing the margins of the ring together with interrupted sutures of chromic catgut, and the retropubic space was drained.

The patient's recovery was complete and he was free of the pain of which he had originally complained. He was discharged from the hospital on March 13, 1951. The wound was well healed at this time.

The patient returned to the hospital on April 6, 1951, stating that the hernia had recurred. Questioning revealed that bulging in the lower end of the scar was present only prior to voiding. The patient stated that when the bladder was full, there was protrusion of a soft mass through the lower end of the incision, but following urination the mass would disappear. Protrusion of the bladder caused abdominal pain and urgency.

Examination revealed a defect in the abdominal wall immediately above the symphysis pubis. With the patient supine, no mass protruded, and in the erect position, no bulging occurred with coughing or straining. When he was examined prior to voiding, however, a soft mass protruded through the ring and hung down over the symphysis. When the bladder was emptied, the mass disappeared. The urine was clear.

On April 7, 1951, the patient was returned to the operating room. An indwelling urethral catheter was introduced into the bladder. The lower midline incision was again opened. The bladder was densely adherent to surrounding structures and lay immediately beneath the skin. The bladder was freed from the anterior rectus sheath and replaced within the

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pelvis. The defect in the fasciai was 5 cm. in diameter, and its edges could not be approximated. A piece of tantalum mesh was cut somewhat larger than the defect and sutured over it with interrupted sutures of tantalum wire. The mesh was sutured to the periosteum of the pubis below, and to the rectus sheath superiorly and laterally. The bladder lay in contact with the under surface of the tantalum mesh. The skin and subcutaneous fat were then closed over the mesh without drainage.

The patient's recovery was uneventful. The indwelling catheter was removed on the fourth postoperative day and the patient voided without difficulty. The wound healed well; there was no collection of fluid beneath the wound. Postoperative examinations of the urine revealed no abnormalities. The patient was discharged April 19, 1951, two weeks after operation.

There has been no recurrence of the hernia.

REFERENCES

1. Koontz, Amos R.: Tantalum Mesh in Hernia Repair: Experimental and Clinical Results, Tr. South. S. A. **60:** 394-403, 1948.
2. Koontz, A. R., and Kimberly, R. C.: Tissue Reactions to Tantalum Mesh and Wire, Ann. Surg. **131:** 666-686, 1950.
3. Koontz, A. R.: Personal communication.

ACUTE CHOLECYSTITIS IN CHILDHOOD

Report of a Case

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A STUDY of acute cholecystitis as it occurs at various ages will disclose that in the neonatal and infancy periods congenital deformities of the biliary tract are the predominant inciting factors, in early childhood the disease has an infectious background, and finally in late adolescence and adult life it is intimately associated with, and frequently secondary to, cholelithiasis.

A comparison of acute cholecystitis in childhood with the same disease in adults provides differences worthy of note. In children, the history of a preceding upper respiratory infection and the frequently obtained positive culture of gall bladder contents suggests a disease of infectious origin.[1] The absence of associated cholelithiasis supports this observation. This is in contrast to acute cholecystitis in adults, in which cholelithiasis is commonly present and is a well-recognized contributing etiological agent.

Diagnosis may be difficult because the history is lacking in elements that suggest gall bladder disease. The localization of findings to the right upper quadrant, however, will necessitate the inclusion of pneumonia, acute appendicitis, intussusception and renal disease in the differential diagnosis. The rarer peptic ulcer and perforated viscus must also be taken into account.

During the past ten years acute cholecystitis in childhood has been less frequently reported than in the ten-year period from 1930-1940. From this one might assume that the frequent use of antimicrobial agents in minor infections has halted the process well in advance of such complications as acute cholecystitis.

A case of acute cholecystitis in a young child is herewith reported which illustrates well some of the features of the disease described above.

CASE REPORT

K. S. (Children's Hospital No. 81129), a 4-year-old white girl, was admitted to Children's Hospital, Columbus, Ohio, on March 15, 1950, with a ten-hour history of severe abdominal pain with nausea and vomiting. The pain began in the right upper quadrant, grew progressively worse, and did not radiate to the back or shoulder. There had been no detectable jaundice. Twenty-four hours prior to admission the patient passed a clay-colored stool, but a subsequent stool passed the day of admission was of normal color and character. Bowel habits had been regular and there was no diarrhea.

The past history was significant for an acute otitis media approximately one week before admission. This had drained spontaneously but was not cultured. The drainage subsided following forty-eight hours of pencillin therapy.

No family history of diarrhea or gall bladder disease could be elicited.

The physical examination disclosed an acutely ill patient with a temperature of 104.8° F., pulse 140, respirations 30. The drum of the left ear was scarred, but no drainage or perforation was apparent. The sclerae were clear, the pharynx benign, and the cervical lymph nodes

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were minimally enlarged. The skin and mucous membranes showed evidence of marked dehydration. The chest was clear, but respirations were rapid and labored. Except for tachycardia, the heart examination was unremarkable. There was acute tenderness and moderate mucular rigidity to light palpation over the entire abdomen, especially marked in the right upper quadrant. No organs could be palpated, and bowel sounds were decreased. On rectal examination, tenderness was noted on either side, but there was no mass, and the stool was brown.

The white blood count was 20,600 with total neutrophils 84 per cent, lymphocytes 16 per cent. The urine was of high specific gravity and contained 3+ acetone. The serum chloride was 102.4 meq. per liter, total base 135 meq. per liter, total serum proteins 6.1 Gr. per 100 c.c. and icteric index normal. Repeat white blood count twelve hours after admission was 24,500 with 91 per cent neutrophils. A flat film of the abdomen was not helpful in the diagnosis. A roentgenogram of the chest was normal.

The possibility of acute appendicitis with perforation could not be excluded. However, the diagnosis was not conclusively established and acute cholecystitis was considered likely. Following admission, the patient was given parenteral fluids to restore hydration and maintain electrolyte balance. Penicillin, 50,000 units every three hours and streptomycin, 0.25 Gm. twice daily were begun. However, since there was no improvement and the white blood count had risen to 24,500, exploratory laparotomy was performed eighteen hours after admission. The abdomen was entered through a right rectus muscle-splitting incision. The gall bladder was found to be injected, edematous, and tightly distended. A trocar was introduced into the fundus and about 40 c.c. of thin yellow pus were aspirated from the gall bladder. Culture of this material yielded *Salmonella oranienburg.** No stones were detectable either before or after decompression of the gall bladder. Because of the critical status of the patient, cholecystectomy was not attempted, and cholecystostomy was performed. Postoperatively, two separate specimens of gall bladder drainage and repeated stool specimens were positive for *S. oranienburg*. These cultures remained positive despite intensive antibiotic therapy of penicillin, 50,000 units every three hours, streptomycin, 0.25 Gm. twice daily, and chloromycetin 0.25 Gm. four times daily. Clinically, the postoperative course was uneventful, and the cholecystostomy tube was removed on the fifth postoperative day. The patient was discharged eleven days after operation to the care of the Public Health Service regarding the "carrier" state. Subsequent stool cultures were positive for three months following discharge from the hospital. Ten months later a cholecystogram depicted a normally functioning gall bladder and a repeat stool culture was negative for Salmonella. The patient had remained free of any abdominal complaints and was able to take an unrestricted diet.

Comment.—In 1938, Potter[3] collected 432 cases of cholecystitis, acute and chronic, below the age of 15 years, 62 per cent of which were in the age group 5 to 15 years, while the remaining 38 per cent were below 5 years of age. It is worth while to note that in this series, fifteen of seventeen patients with acute cholecystitis, gangrene, and perforation were found to have typhoid (*Salmonella typhosa*) as the etiological agent.

In addition to the usual gastroenteric manifestations, it is not uncommon to find the Salmonella organism as a cause of peritonitis,[6] osteomyelitis,[5] meningitis[4] and salpingitis.[11]

Salmonella cholecystitis in adults is occasionally reported,[6, 7, 11, 12] but this disease in children is especially rare. Seligmann and co-workers[7] reported 2,000 cases of Salmonella infections, only ten of which represented cholecystitis; all were in adults. Further, forty-four cases of cholecystitis from this type of organism are on file in the National Salmonella Center of New York City,[8] but the youngest occurred in a boy sixteen years of age.

*Isolated by the Michigan State Salmonella Laboratory.

On the other hand, Salmonella infections in general occur frequently in very young individuals in both human beings and animals. The presence of bile is not adverse to the growth of the Salmonella organisms, but rather is often used in its culture and isolation. It is, then, conceivable that the gall bladder may be susceptible to Salmonella infection in either the clinical or carrier state. Edwards and co-workers,[9, 10] in a summary of eighty-six cases in which Salmonella was isolated from extraintestinal sources, found the organisms in the gall bladder in eight cases. None of these were *S. oranienburg* strains. The latter organism has been isolated from such extraintestinal sources as the spinal fluid, endocardium, and wounds.[10] The case reported here represents one of acute cholecystitis due to *S. oranienburg*.

SUMMARY

1. A discussion of the salient features of acute cholecystitis in childhood is briefly presented.

2. A case of acute cholecystitis due to *Salmonella oranienburg* in a four-year-old girl is presented in detail.

3. Salmonella infections as related to gall bladder disease are discussed.

REFERENCES

1. Montgomery, A. H.: Disease of the Gallbladder in Children, Am. J. Dis. Child. **44**: 372-375, 1932.
2. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, 1941, W. B. Saunders Company, pp. 287-289.
3. Potter, A. H.: Biliary Disease in Young Subjects, Surg., Gynec. & Obst. **66**: 604-610, 1938.
4. Guthrie, K. J., and Montgomery, G. L.: Infections with Bacterium Enteritides in Infancy with the Triad of Enteritis, Cholecystitis, and Meningitis, J. Path. & Bact. **49**: 393, 1939.
5. Razansky, R., Ehrenfeld, E. N., and Matloth, Y.: Paratyphoid Osteomyelitis, Two Cases, Brit. M. J. **2**: 297-298, 1948.
6. Bender, C. E.: Salmonella Fever: Report of Five Cases, One Complicated by Cholecystitis, Perforation and Peritonitis with Autopsy Findings, Northwest Med. **45**: 660-665, 1940.
7. Seligmann, E., Saphra, Ivan, and Wasserman, M.: Salmonella Infections in the USA: A Second Series of 2,000 Human Infections Recorded by the New York Salmonella Center, J. Immunol. **54**: 69-87, 1946.
8. Seligmann, E.: Personal communication.
9. Edwards, P. R., Bruner, D. W., and Moran, A. B.: Further Studies on the Occurrence and Distribution of Salmonella Types in the United States, J. Infect. Dis. **83**: 220-231, 1948.
10. Edwards, P. R., Bruner, D. W., and Moran, A. B.: The Genus Salmonella: Its Occurrence and Distribution in the United States, Lexington, Ky., 1948, Bull. 525, Kentucky Agriculture Experiment Station.
11. Jager, B. V., and Lamb, M. E.: Sporadic Infections Carried by Salmonella Suipestifer and Salmonella Oranienburg, New England J. Med. **228**: 299-305, 1943.
12. Walker, I. J., Weiss, S., and Nye, R. N.: Salmonella Suipestifer Infection with Surgical Complication, New England J. Med. **214**: 567-571, 1936.

Recent Advances in Surgery

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CHOLECYSTITIS IN CHILDHOOD; ASSOCIATED OBSTRUCTIVE JAUNDICE

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CHOLECYSTITIS in childhood was first reported in 1722 by Gibson.[1] Subsequently, there have been published reports of at least 474 cases; of these only 19 were associated with choledocholithiasis. Nevertheless, our review of gall bladder disease in the very young population revealed a striking incidence of jaundice. Over a decade ago, this subject received no attention in pediatric teaching or in surgical considerations of biliary tract disease. Cholecystitis in childhood was thought too rare, its clinical implications too insignificant, to merit even passing mention. Potter,[2] by his vigorous review in 1938, popularized the subject in some measure. According to this most widely quoted source, cholecystitis in childhood was important: the condition was more frequent than suspected and often overlooked. We cannot agree that the disease is important because of an increased incidence. Evidence at hand does not support the view that true primary biliary tract disease in children is not infrequent. Rather we would suggest that the disease should receive some thought in the differential diagnosis of abdominal pain and jaundice in children.

Our own case[3] stimulated an investigation of the true clinical importance of gall bladder disease in children. The practical concern was with a condition, connoting pathologic changes, similar to that in the adult, primarily cholecystitis with or without cholelithiasis. We recognized the possible existence of associated and subsequent pathologic processes ranging from carcinoma of the gall bladder to common duct obstruction. In our review, incontravertible proof of the presence of disease in the gall bladder included the results of gross and microscopic examination. We accepted gross description at the operating table (especially presence of calculi) if it correlated with the clinical findings and any other pathologic changes present. Rejected as not having true cholecystitis, were those patients not operated upon whose condition more properly fell into the classification of hepatitis and disease associated with prehepatic jaundice. We did not accept as bona fide cholecystitis those cases reported on the basis of symptoms only, or on the basis of the Graham-Cole test reporting a nonfunctioning gall bladder. In children with infectious disease accompanied by pyrexia, dehydration, or starvation; or in those patients whose actually reported disease was perforated appendicitis with peritonitis, we did not accept as proof

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of cholecystitis a "distended gall bladder that would not empty" or one filled with "thick dark bile." For the purpose of this review, our concern embraced infancy, childhood, and early adolescence. We decided that the neonatal period with its congenital defects of the biliary tract did not belong in this discussion of cholecystitis. To keep the real picture of age incidence more accurate, we elected to designate children 15 years of age or younger, who have attained puberty, as early adolescents.

With these qualifications in mind, we reviewed the case reports in the literature[4-35] available to us up to 1948 (Tables I and II). A critical study of these cases, as well as the 432 reported prior to 1938, revealed that not all were substantially proved. Accordingly, we based our analysis on the reports that submitted adequate data and were acceptable on the basis of the aforementioned criteria.

TABLE I

	CASES REPORTED	ACCEPTABLE CASES
Potter[33] (1722 to 1927)	226	176
Potter[2] (additional to 1927)	44	31
Potter[2] (1928 to 1937)	162	89
Present report (1938 to 1948)	43	30
Total	475	326

Of the 30 acceptable cases reported in the decade 1938 to 1948, 18 (60 per cent) of the patients had cholelithiasis, 2 (7 per cent) had choledocholithiasis, and 13 (43.3 per cent) were complicated by jaundice (Tables III and IV). There was 1 case of acute cholecystitis associated with typhoid fever in which no calculi were present. In the 2 patients with common duct stones 1 (Case 3) gave no history of jaundice and no icterus was discovered when studied in the hospital; the other (Case 30) gave a history of jaundice, but presented no icterus when studied in the hospital. Twenty-four of the cases were diagnosed correctly by clinical work-ups. However, many of the cases of jaundice were at one time or another considered "infectious hepatitis." Preoperatively, 5 of the 30 cases were diagnosed incorrectly as acute appendicitis. However, in all 5, the correct diagnosis was made at the operating table by alert surgeons. One child's condition was misdiagnosed "catarrhal jaundice" and the patient not operated upon; the diagnosis of cholecystitis was established at necropsy.

To consult other clinics about their experience, we communicated with 25 authorities with a wide geographical distribution. The replies from 21 correspondents were analyzed. Many of the surgical and pediatric authorities had no personal experience or firsthand knowledge of a child with proved primary gall bladder disease. Among these were H. L. Bockus, Philadelphia; I. S. Ravdin, Philadelphia; F. H. Lahey, Boston; O. Swenson, Boston; S. Farber, Boston; L. Schiff, Cincinnati; W. M. Firor, Baltimore; M. Ravitch, Baltimore; W. P. Longmire, Jr., Los Angeles; M. Thorek, Chicago; and R. Elman, St. Louis. Ravitch noted that they had had experiences with cholelithiasis in association with sickle-cell anemia and familial hemolytic icterus. Ravdin operated upon a boy with stones in the gall bladder and common bile duct who

TABLE II. CHOLECYSTITIS IN

CASE	AUTHORS	SEX AND AGE	HISTORY	JAUNDICE
1.	Linden, E. K.[4]	Female 8 yr.	Abdominal pain, no fever	None
2.	Linden, E. K.[4]	Female 11 yr.	Abdominal pain for a few months with jaundice, acholic stools	Not on admission
3.	Linden, E. K.[4]	Male 12 yr.	Abdominal pain since 6 years old with flatulent indigestion	None
4.	Rivara, L. T., and Cerdeiro, A. M.[5]	Male 7 yr.	Diagnosis acute appendicitis; abdominal pain 2 days with some tenderness in R.U.Q.	None
5.	Rivara, L. T., and Cerdeiro, A. M.[5]	Male 8 yr.	Abdominal pain	None
6.	Clavel, C., and Dumas, J.[6]	Male 8 yr.	Acute onset of abdominal pain; vomiting	None
7.	Chen, S. C.[7]	Male 6 yr. (Chinese)	Chilliness, fever 10 days' duration; pain in R.U.Q. of 4 days' duration	Yes
8.	Boesman, T.[8]	2 yr.	Suffered from ascaris infection with indigestion	None
9.	Luzuy, M., and Audy[9]	Male 3 yr.	Abdominal pain with vomiting; diagnosis of acute appendicitis made	None
10.	Sallick, M. A.[10]	Female 12 yr.	Epigastric pain, 3 days' duration; pain shifted to R.U.Q.; had 3 other attacks in past year with jaundice	Not on admission
11.	Carmichel, J. L.[11]	Male 4 yr. (Negro)	Abdominal pain intermittent for several days; mother noted mass in R.U.Q.	None
12.	Bisson, C.[12]	Female 9 yr.	Onset of vomiting; abdominal pain	None
13.	Tearman, R. A.[13]	Male 10 yr.	Several weeks' duration of pain in R.U.Q.	None
14.	Notti, H. J., Ferrer, H., and Grinfeld, A.[14]	Male 11 yr.	R.U.Q. pain, tenderness during attack of typhoid fever	None
15.	Melchior, E.[15]	Female 14 yr.	History, R.U.Q. pain with jaundice	Yes

CHILDHOOD, 1938 TO 1948

DIAGNOSIS	OPERATION	STONES	PATHOLOGIC REPORT	REMARKS
1. History and physical examination 2. X-ray flat plate showed stones	Cholecystectomy	In gall bladder	Cholecystitis, subacute	Improved
1. History and physical examination 2. X-ray	Cholecystectomy	In gall bladder	Cholecystitis, subacute	Improved
1. History and physical examination 2. X-ray	Cholecystectomy, choledochostomy	In gall bladder and common duct	Cholecystitis, acute	Improved
1. Clinical signs of appendicitis with some tenderness in R.U.Q.	Appendectomy, cholecystectomy	One in gall bladder	Acute cholecystitis with cholelithiasis	Operated for appendicitis, appendix removed; gall bladder inflamed and cholecystectomy performed; improved
1. Clinical signs of appendicitis 2. At operation gall bladder found inflamed	Cholecystectomy	In gall bladder	Cholecystitis, acute, with cholelithiasis	Improved
1. History of indigestion 2. Tenderness R.U.Q	Cholecystostomy	Yes	None	Improved
1. History and palpation of a mass in R.U.Q. 2. Leucocytosis, jaundice	Cholecystostomy	None	None	At operation the gall bladder was distended and contained pus; improved
1. History and physical examination	Cholecystectomy	None	Acute, purulent cholecystitis	Believed that ascaris blocked the cystic or common duct; improved
1. Diagnosis, acute appendicitis 2. Bile present in peritoneal cavity	Cholecystectomy	None	Acute cholecystitis with perforation	Improved
1. History 2. Physical examination	Cholecystectomy	In gall bladder	Gall bladder thickened, acutely inflamed	Improved
1. History and physical examination, mass size of lemon 1 inch above and to the right of the navel	Cholecystectomy	No	1. Marked engorgement, edema 2. Subacute cholecystitis	Improved
1. History 2. Tenderness with rigidity in R.U.Q. 3. 24,000 w.b.c.	Cholecystostomy	In gall bladder	None	Improved
1. "Clinical grounds"	Cholecystostomy	1,000 in gall bladder	None	Recovery uneventful
1. Operation	Cholecystostomy	No	Perforated gall bladder, acute, suppurative	Improved
1. History 2. Physical examination	Cholecystectomy	In gall bladder	Empyema of gall bladder	Improved

TABLE II

CASE	AUTHORS	SEX AND AGE	HISTORY	JAUNDICE
16.	Melchior, E.[15]	Male 13 yr.	Flatulent indigestion for several years; acute onset R.U.Q. pain	None
17.	Seidler, V. B., and Brakeley, E.[16]	Female 10 yr. (Negro)	Two weeks' duration of weakness, jaundice; attacks of jaundice since age of 4 yr. No typical biliary colic	Yes
18.	Rivas Diez, B.[17]	Female 11 yr.	History abdominal pain with nausea, vomiting, jaundice of 3 days' duration	Yes
19.	Jaroslavsky, L. and Blumenfeld, I.[18]	Female 13 yr.	Acute onset, epigastric pain, nausea, vomiting	None
20.	Van Staveren, C.[19]	Male 7 yr.	Periodic attacks of indigestion, epigastric pain, nausea, flatulence, jaundice	Yes
21.	Sobel, I. P.[20]	Female 6 yr.	Painless, increasing jaundice for 1 week; hospitalized for several weeks and then discharged with diagnosis of "catarrhal jaundice"	Yes
22.	Penberthy, G. C., and Benson, C. D.[21]	Female 11 yr.	Epigastric, R.U.Q. pain of 3 weeks' duration with jaundice of 3 weeks, palpable liver, tenderness in R.U.Q.	Yes
23.	Penberthy, G. C., and Benson, C. D.[21]	Male 10 yr.	R.U.Q. pain with intermittent jaundice, 2 years' duration; symptoms after scarlet fever	Yes
24.	Narat, J. K.[22]	Male 4 yr.	Abdominal pain of 4 days' duration; tenderness in R.U.Q.	None
25.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Female 13 yr.	Recurrent attacks of R.U.Q. pain, nausea, vomiting, fever	None
26.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Male 6 yr.	Onset R.U.Q. pain during attack of lobar pneumonia	None
27.	Ashley, L. B., and Narotzky, A. S.[24]	Male 4 yr.	Acute onset of abdominal pain, nausea, vomiting 2 days prior to admission	Yes
28.	Bogatko, F. H., and Mehlman, J.[25]	Male 3 yr.	Jaundice at 1 year of age; abdominal pain, jaundice at present admission	Yes, 6 weeks
29.	Heringman, E. C., and Aiken, D. W.[26]	Male 7 yr.	Generalized abdominal pain 7 hours' duration	No
30.	Ulin, A. W., Nosal, J. L., and Martin, W. L.[3]	Female 13 yr.	Recurrent attacks abdominal pain and jaundice	History, yes; not on admission

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DIAGNOSIS	OPERATION	STONES	PATHOLOGIC REPORT	REMARKS
1. History 2. Physical examination	Cholecystectomy	In gall bladder	Gangrenous gall bladder	Improved
1. History and physical examination 2. X-ray showed stones	Cholecystectomy	Many in gall bladder	Cholecystitis, acute	At operation, gall bladder was inflamed and contained many stones; improved
1. History 2. X-ray showed nonvisualizing gall bladder	Cholecystectomy, appendectomy	In gall bladder	Cholecystitis with cholelithiasis	Improved
1. History and physical examination	Cholecystectomy, appendectomy	100 in gall bladder	Cholecystitis with cholelithiasis	Improved
1. Family history of gall bladder disease 2. Physical examination	Cholecystectomy	In gall bladder	Enlarged gall bladder with stones	Improved
1. Readmitted 3 months later with recurrent painless jaundice	None	Yes, at necropsy	Patient died on 115th day of illness; necropsy showed gangrenous gall bladder with one large stone, enlarged liver, dilated common duct	Died on 115th day of illness
1. Made on clinical signs and symptoms	Cholecystostomy	None	Subacute cholecystitis; gall bladder distended	Improved
1. History and physical signs of jaundice, palpable liver, tenderness in R.U.Q.	Cholecystostomy	None	Subacute cholecystitis; gall bladder distended and thickened	Improved
1. Symptoms and physical findings	Aspiration of gall bladder performed	None	Greatly distended gall bladder; contained serous, viscid fluid, nearly colorless	Improved
1. History 2. Tenderness R.U.Q. 3. X-ray normal	Cholecystectomy	None	Gall bladder thickened, distended	Improved
1. Tenderness, rigidity in R.U.Q.	Cholecystectomy; thoracotomy for pleural empyema	None	Gall bladder thick and distended	Recovery following operation
1. Acute appendicitis	Cholecystostomy	None	Acute gangrenous cholecystitis	
1. History 2. Laboratory work indicated obstructice jaundice	1. Choledochostomy 2. Cholecystectomy 4 weeks later	Gravel in gall bladder	Diverticulum with gall bladder, chronic inflammation	Congenital anomaly of gall bladder; improved
1. Tenderness in the R.U.Q.	Appendectomy, cholecystectomy	None	Subacute and chronic cholecystitis	Preoperative diagnosis was appendicitis; improved; doubtful case?
1. History 2. Tenderness 3. X-ray	Cholecystectomy, choledochostomy	In gall bladder and common duct	Cholecystitis, subacute	Improved

TABLE II

CASE	AUTHORS	SEX AND AGE	HISTORY	JAUNDICE
31.	Burke, E. C., and Platou, E. S.[27]	Male 10 wk.	Jaundice 2nd day after birth, with acholic stools	Yes; cleared up after 78 days in hospital
32.	Burke, E. C., and Platou, E. S.[27]	Male 2 dy.	Convulsions, cyanosis, erruption	Yes
33.	Acuna, J., and Accinelli, A. A.[28]			
34.	Chiodin, L., and Belizan, L. A.[29]			
35.	Downie, V. J.[30]	Male 15 mo.	Vomiting and diarrhea of 9 days' duration	None
36.	Swing, A. T., and Bullowa, J. G. M.[31]	Male 13 yr. (Negro)	Scarlet fever: during recuperation, developed acute abdomen; diagnosis of ruptured appendix made	None
37.	Swing, A. T., and Bullowa, J. G. M.[31]	Male 9 yr.	21st day of scarlet fever, developed abdominal pain, jaundice; conservative treatment	Yes
38.	Recalde Cuestas, J. C., and Tejerina Fotheringham, W.[32]			
39.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Female 13 yr.	Recurrent attacks of R.U.Q. pain, nausea, vomiting, fever	None
40.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Female 15 yr.	Recurrent attacks of R.U.Q. pain	None
41.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Female 11 yr.	Severe attacks of R.U.Q. pain, possible jaundice	Questionable on admission
42.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Male 12 yr.	Recurrent attacks of abdominal pain, nausea, and vomiting	None
43.	Lowenburg, H., Jr., and Mitchel, A. G.[23]	Female 12 yr.	Recurrent R.U.Q. pain, nausea, vomiting, chills	None

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DIAGNOSIS	OPERATION	STONES	PATHOLOGIC REPORT	REMARKS
1. History 2. Physical examination—jaundice; temperature normal; enlarged spleen	None	None	None	It was assumed biliary radicles were plugged with inspissated bile; certainly not a proved case; improved
1. History 2. Physical findings	Cholecystostomy	None	None	Improved; doubtful case No data available No data available
1. Patient listless, toxic with tenderness in R.U.Q.; diagnosis of appendicitis made	Cholecystostomy	None	None	Operation for appendicitis; gall bladder thick, large; improved; not a proved case
1. History as recorded 2. At operation gall bladder was distended	Abdomen was just opened and closed; nothing done	None	None	Improved; perforated appendicitis; not a cholecystitis
1. Diagnosis made on clinical grounds	No operation	None	None	Improved; not a valid case No data available
1. History 2. Tenderness, rigidity in R.U.Q. 3. Gall bladder not visualized by x-ray	Appendectomy	None	Gall bladder distended	Improved; doubtful case
1. Marked general abdominal tenderness, rigidity R.U.Q. 2. X-ray showed nonvisualization of gall bladder	Appendectomy	None	Gall bladder distended	Improved; not a proved case of cholecystitis
1. Symptoms 2. Tenderness, rigidity in R.U.Q., and jaundice	Appendectomy	None	Gall bladder distended	Improved; doubtful case
1. Extreme tenderness in R.U.Q. 2. X-ray, gall bladder not visualized	Cholecystectomy	None	Biliary drainage: bile turbid; leucocytosis; numerous motile Lamblia intestinalis	At operation: chronic adhesive perisplenitis, peritonitis, hepatitis, adhesions at the base of the gall bladder, liver enlarged; improved
1. History 2. Rigidity, mass in R.U.Q.	None	None	None	Recovery following biliary drainage; not a proved case of cholecystitis

had hemolytic anemia. W. Walters reported that at the Mayo Clinic they had had an incidence of cholelithiasis in children of 1.3 per thousand adult cases. Presumably most, if not all, of these childhood cases were associated with hemolytic disease. C. Sweet of Oakland, Calif., described two cases of cholelithiasis, but neither one was proved.

TABLE III. TEN CASES OF JAUNDICE ON ADMISSION, 1938 TO 1948. (NONE HAD COMMON DUCT STONE)

NUMBER OF PATIENTS	
1	Died—mistaken diagnosis of hepatitis; this patient had an acute gangrenous cholecystitis and cholelithiasis; the common duct was dilated
9	Common duct not explored; no evidence of common duct stones
4	No stones
	1 acute gangrenous cholecystitis
	2 subacute cholecystitis
	1 empyema of gall bladder
5	Gall stones
	1 empyema of gall bladder
	3 acute cholecystitis
	1 chronic cholecystitis
Nine out of ten patients who had jaundice on admission had an acute inflammatory process in the gall bladder	
Four out of ten had no stones in the gall bladder or common duct	

TABLE IV. THIRTY CASES, 1938 TO 1948

	NUMBER OF PATIENTS	RESULTS
Sex Incidence		
Males	17	
Females	12	
Not stated	1	
Age Incidence		
1 to 5 years	6	
6 to 9 years	10	
10 years	3	
11 years	5	
12 years	2	
13 years	3	
14 years	1	
20% were 12 to 15 years of age		
47% were 10 to 15 years of age*		
Operation and Result		
Cholecystostomy	10	Recovered
Cholecystectomy	17	Recovered
Cholecystectomy and choledochostomy	2	Recovered
Not operated	1	Died

*In Potter's 1928 review,[33] 38 per cent were 10 to 15 years old; in his 1938 review,[2] 31 per cent were 10 to 15 years old.

The men who reported definitely verified childhood cholecystitis were Hamilton Bailey, London; Rodney Maingot, London; H. Glenn Bell, San Francisco; C. F. McKhann, Cleveland; Moses Behrend, Philadelphia; James Baty, Boston; Donald Brayton, Los Angeles; Dorothy Anderson and Norman E. France of New York City. There were 42 cases of cholecystitis reported to us. However, on the basis of our criteria, only 14 cases were acceptable as proved.

In 7 patients a positive statement concerning icterus was made; of these, 3 gave a history of jaundice. In 9 cases, the sex was noted: 5 female, 4 male. The report from Anderson and France was interesting because it coincided with the general picture in the literature of biliary tract disease in the young. About 20 per cent of the cases were due to congenital defects of the biliary system. In over one-half of the cases where cholecystitis was incidental to another disease, the prognosis was very poor. These cases were picked up at autopsy and apparently the cholelithiasis did not contribute to the mortality. Similarly, Brayton's data disclosed that few of the cases he reported were primarily true cholecystitis. His first case was of interest in that empyema of the gall bladder was secondary to a perforated appendix. Others in the literature reported pathologic changes in the bile and gall bladder incidental to or subsequent to, appendicitis and peritonitis. These cases were not all well documented so that one could draw no conclusions. However, the evidence suggested that in a very sick child, regardless of the primary disease, there might be enough alteration in the physiology of the biliary tract to make acute cholecystitis a possibility as an important complication.

DISCUSSION

Our concept of childhood cholecystitis is based on a review of 326 valid cases reported in the literature, as well as on the experience of our correspondents. As general surgeons, we found it instructive and of great interest to contrast the childhood disease with adult cholecystitis. Some of the outstanding features of this analysis are listed in Table V.

The etiology of cholecystitis[36, 37] and the cause of gall stones in childhood remain just as obscure as in the adult. Probably no single factor is completely

TABLE V. COMPARISON OF CHOLECYSTITIS, CHILDHOOD AND ADULT DISEASE

	CHILDHOOD	ADULT[63-67]
Average age of onset	8 to 10 years	29 to 36 years
History	Significant story of chronic dyspepsia not common; may be obtained in the older, more articulate child	
Clinical signs	Similar to acute disease in the adult	
Sex	Male, about 3 to 2	Female, 4 to 1
Jaundice*	26 to 45%	8 to 10%
Gall bladder stones	57 to 69%	80 to 95%
Common duct stones	6%	17%
Jaundiced cases*	92% (no common duct stones)	53% (no common duct stones)
Pathology	Usually microscopic sections show more infiltration with polymorphonuclear leucocytes and evidence of acute inflammation; bacteria may be seen in the gall bladder wall	Even in clinically acute cases, the microscopic sections often reveal a picture of chronic inflammation; one rarely sees bacteria in the stained sections
Associated gall bladder malignancy	2 of 326 cases; less than 1%	Incidence 1 to 3%
Surgery	Results excellent; need for exploring common duct apparently not as urgent	Residual stones in common duct a major problem

*Not necessarily on admission, but with a definite recent history of icterus.

responsible; perhaps, in most cases, two or more factors are associated in producing the pathologic changes. In the adult disease[38-41] the factors that are usually considered are: (1) functional—obstruction of biliary passages by spasm, mass, concretions, and so on; (2) metabolic—possibly associated with primary hepatic dysfunction, changes in nature and quantitative constituents of bile, disturbances in the cholesterol metabolism, hemolytic disease, dietary habits; (3) infection—systemic, gastrointestinal. One predisposing factor in the adult is sex, female predominating 3 or 4 to 1. In the child, this ratio does not hold. Furthermore, in the acceptable cases, gall stones occurred in only 57 per cent of the children. The impression is that in the etiology of the childhood disease, there has been more of an association with acute infections, especially typhoid fever.[42, 43] Scarlet fever and measles may play a leading part in the etiology. However, if this is so, we should certainly see more cases of gall bladder disease among children. Swing and Bullowa[31] reported a series of 12,352 cases of scarlet fever with 2 cases of acute cholecystitis. Neither one of these was proved. The differences between childhood and adult cholecystitis emphasized in this report (Table V) do not necessarily argue for differences in etiologic factors; they do indicate however, a different interplay of the factors involved.

Microscopically, in the adult disease, varying degrees of edema, congestion, necrosis, and infiltration of the wall with lymphocytes and monocytes are seen. Even in extreme degrees of inflammation, neutrophils may be uncommon and bacteria are seldom found in sections of the wall. However, in our review of pathologic reports in cases of primary or incidental cholecystitis in childhood we found that polymorphonuclear leucocytes are likely to be present in the acute disease. In some instances, the sections showed the presence of bacteria. The low incidence of common duct stone and yet the high frequency of jaundice is of interest. In the jaundiced patients the obstructive process was usually associated with a very acute or suppurative process in the gall bladder. In 2 cases an acutely inflamed diverticulum of the common duct produced obstructive jaundice; in 2 other cases, inflammatory lymphadenopathy obstructed the common duct. The general trend of the information we have collected seems to indicate that infection, locally and systemically, plays a more important part in childhood cholecystitis than in that of the adult. Jaundice in most of the cases in childhood is due in some way to an acute inflammatory process adjacent to or involving the ducts, and not to common duct stone. The duration of the disease in the adult is longer, marked by chronicity and episodes of recurrence and exacerbation, and this may explain why the incidence of common duct stones is higher. Finally, there were 2 cases of cancer of the gall bladder[44, 45, 46] among the 326 acceptable cases. This compares with the incidence of 1 to 3 per cent in adult cholecystitis. Of interest pathologically are the number of childhood cases of cholelithiasis discovered incidentally at post mortem and at operation. Many of these patients have distended gall bladders with no evidence of real inflammation in the wall. The calculi, when described, number 1 or 2; they are friable, dark green, irregular concretions measuring 2 mm., or at the most 3

mm., in diameter. They may be associated with a dark, sandy bile. Then again, the cases of spherocytic jaundice illustrate the possibility of stone formation in the gall bladder without the presence of inflammation in the wall, emphasizing the effect of metabolic factors in the etiology and pathology of cholelithiasis.

It is interesting to note that in 15 per cent of the cases the diagnosis was erroneously made as acute appendicitis. This is no doubt due to the fact that children do not localize their pains accurately and that gall bladder disease is not usually thought of as occurring in a child. Some authors believe that the clinical picture[47-57] differs in some respects from that seen in the adult. There have been cases with epigastric pain and periumbilical tenderness. The same can be said of adult cases; not all are so-called typical. However, in reviewing the reports, one is impressed with the fact that most childhood cases resemble very closely in their signs and symptoms those seen in adult life. When the child is old enough and is cooperative, usually the story he gives of the pain and its radiation is typical of gall bladder disease. The appearance of jaundice has in many instances confused the diagnosis with hepatitis; however, in the majority of these cases the correct conclusion was reached eventually.

In addition to the history and physical findings, scout film of the abdomen, visualization of the gall bladder with dye,[16, 58] and duodenal drainage[59] will assist in establishing the diagnosis. In the presence of jaundice, the various tests associated with the study of hepatocellular disease as well as hemolytic disease are mandatory. Children with undiagnosed recurrent abdominal pain and dyspepsia should receive a work-up to exclude gall bladder disease as well as peptic ulcer. Bird and associates[60] have stressed the importance of a gastrointestinal series to help solve some of these obscure abdominal cases.

The principles of gall bladder surgery as practiced upon adults[61-67] apply also to children. The record shows that children will stand this type of surgery very well. Cholecystectomy is the treatment of choice. Early operation, when the diagnosis is established and the patient well prepared, is often the safest course of management. Indications for exploring the common duct exist; however, the history or presence of jaundice itself may not make choledochostomy mandatory (Table III). Of interest is the report of Edington[68] who did a cholecystostomy in a child. The patient had recurrent symptoms that several years later required cholecystectomy.

CONCLUSIONS

Our review of childhood cholecystitis indicates that the disease is very uncommon, probably rare. Certainly choledocholithiasis is rare. However, when the disease is suspected the correct diagnosis is most often eventually made. Surgical treatment is relatively easy and attended by excellent results. Therefore, it is important that physicians, when confronted with a case of cholecystitis in a child, should not be incredulous, or reject such a diagnosis.

It is only fair to state that there may be children with undiagnosed, recurrent abdominal pain of obscure origin not suspected of gall bladder disease or studied for it, whose cases are diagnosed as such, years later. These are the

children we should suspect of gall bladder disease and perhaps peptic ulcer, and work up diagnostically, utilizing diagnostic measures employed with the adult. Also, in the past decade, 5 out of 29 operated cases were diagnosed by the surgeon at the operating table. When we operate for appendicitis in a child and find no disease in the lower abdomen, should we not palpate or inspect the right upper quadrant?

There is pathologic evidence that cholecystitis in the child may be incidental to serious illness—peritonitis, meningitis, pneumonia, and so on. Most of this was revealed at necropsy; the biliary tract disease did not cause the mortality. However, clinically, this possibility should be kept in mind as it may contribute to the cause of death.

Also, pediatricians and general practitioners intent on considerations of hepatitis, jaundice, and the differential diagnosis of abdominal disease should consider the possibility of cholecystitis and cholelithiasis. Our own case, as well as others complicated by jaundice and misdiagnosed as "catarrhal jaundice," suggests that perhaps cholecystography should be done during some phase of the illness, in cases diagnosed as hepatitis. Gall bladder disease in the child is a more acute inflammatory condition than that which we ordinarily encounter in the adult. In the child there is a far greater incidence of obstructive jaundice without presence of calculus in the common duct. This may be related to the more acute process adjacent to the common duct; or perhaps, in some instances, common duct stones occur but are passed more readily in the child.

Physicians should remember that jaundice of hepatocellular origin is the more common and more important disease. Ill-advised surgery in this condition may lead to an increased mortality.

SUMMARY

1. The problem of cholecystitis in childhood is defined from the point of view of incidence and differential diagnosis. The significance of jaundice in these cases is emphasized.

2. The literature on the subject is brought up to date and critically analyzed. Case reports from 1938 to 1948 are listed.

3. The experience of 21 contemporary authorities is recounted.

4. Brief remarks are presented on pathology, etiology, clinical picture, diagnosis, and treatment of cholecystitis in childhood.

5. Cholecystitis in childhood is contrasted with the adult disease.

REFERENCES

1. Gibson, J.: Medical Essays and Observations, 1722. Quoted by Snyder, C. C.: Cholecystitis and Cholelithiasis in Young Children, J. A. M. A. 85: 31, 1925. (Necropsy quoted by Sobel.[20])
2. Potter, A. H.: Biliary Disease in Young Subjects, Surg., Gynec. & Obst. 66: 604-610, 1938.
3. Ulin, A. W., Nosal, J. L., and Martin, W. L.: Cholecystitis in Childhood; Case Report. J. A. M. A. To be published.
4. Linden, E. K.: Biliary Tract Disease in Children, Acta. chir. Scandinav. 89: 446-452, 1943.
5. Rivara, L. T., and Cerdeiro, A. M.: Litiasis biliar en la infancia, Semana méd. 2: 870-875, 1941.

6. Clavel, C., and Dumas J.: La cholécystite calculeuse aigue chez l'enfant, Lyon chir. **41:** 411-429, 1946.
7. Chen, S. C.: Empyema of Gall-bladder in a Child, Brit. M. J. **1:** 567, 1947.
8. Boesman, T.: Empyema of Gallbladder in Young Child; Case, Nederl. tijdschr. v. geneesk. **90:** 1619-1621, 1946.
9. Luzuy, M., and Audy: Perforation de la vésicule biliaire en péritoine libre chez un enfant de trois ans. Cholécystectomie subtotale. Guérison, Mém. Acad. de chir. **71:** 26-28, 1945.
10. Sallick, M. A.: Cholecystitis and Cholelithiasis in Childhood, J. Mt. Sinai Hosp. **9:** 963-966, 1943.
11. Carmichel, J. L.: Gallbladder Disease in Children; Short Review of Literature With Case Report, J. M. A. Alabama **12:** 225-227, 1943.
12. Bisson, C.: La cholécystite calculeuse chez l'enfant, Union méd. du Canada **71:** 45, 1942.
13. Tearnan, R. A.: Cholecystitis and Cholelithiasis in Children; Report of a Case, Illinois M. J. **79:** 418-421, 1941.
14. Notti, H. J., Ferrer, H., and Grinfeld, A.: La litiasis biliar en la infancia, Arch. argent. de pediat. **11:** 167-174, 1940.
15. Melchior, E.: Gallensteinerkrankungen im Kindesalter, Ann. paediat. **154:** 292-295, 1940.
16. Seidler, V. B., and Brakeley, E.: Gallstones in Children; Report of a Case Diagnosed by Roentgen Examination and Confirmed at Operation, J. A. M. A. **114:** 2082-2085, 1940.
17. Rivas Diez, B.: Colecistitis calculosa en una niña de 11 años de edad, Semana méd. **1:** 37-39, 1939.
18. Jaroslavsky, L., and Blumenfeld, I.: Litiasis biliar precoz en una niña, Semana méd. **2:** 1506-1509, 1938.
19. Van Staveren, C.: Acute Cholecystitis in Young Children, Nederl. tijdschr. v. geneesk. **83:** 4115-4117, 1939.
20. Sobel, I. P.: Cholecystitis and Cholelithiasis in Childhood; Report of Case, Arch. Pediat. **55:** 669-681, 1938.
21. Penberthy, G. C., and Benson, C. D.: Surgery of the Biliary Tract in Infants and Children, Am. J. Surg. **40:** 232-236, 1938.
22. Narat, J. K.: Hydrops of Gall-bladder in a 4 Year Old Child, Am. J. Surg. **49:** 513-514, 1940.
23. Lowenburg, H., Jr., and Mitchel, A. G.: Cholecystitis in Childhood, J. Pediat. **12:** 203-208, 1938.
24. Ashley, L. B., and Narotzky, A. S.: Acute Gangrenous Cholecystitis in Children; Report of a Case in a Child Aged 4, J. Michigan M. Soc. **40:** 287, 1941.
25. Bogatko, F. H., and Mehlman, J.: Cholecystitis and Cholelithiasis in a Congenital Diverticulum of the Gall bladder in a Three-Year old Boy, J. Pediat. **31:** 75, 1947.
26. Heringman, E. C., and Aiken, D. W.: Cholecystitis and Cholelithiasis in the Young, Am. J. Surg. **74:** 27-32, 1947.
27. Burke, E. C., and Platou, E. S.: Biliary Obstruction in Newborn With Recovery, Journal Lancet **66:** 232-235, 1946.
28. Acuna, J., and Accinelli, A. A.: Consideraciones sobre litiasis biliar en la infancia, Arch. argent. de pediat. **15:** 31-36, 1941.
29. Chiodin, L., and Belizan, L. A.: Colecistitis calculosa en un niño, Bol. Soc. de. cir. de Rosario **6:** 121-126, 1939.
30. Downie, V. J.: Case of Acute Cholecystitis Occurring in an Infant, Brit. J. Surg. **25:** 914-915, 1938.
31. Swing, A. T., and Bullowa, J. G. M.: Acute Cholecystitis Complicating Scarlet Fever, Am. J. Dis. Child. **55:** 521-525, 1938.
32. Recalde Cuestas, J. C., and Tejerina Fotheringham, W.: Colecistitis crónica no calculosa en una niña de 5 años. Colecistectomiá, Rev. Soc. pediat. de Rosario **5:** 129-133, 1940.
33. Potter, A. H.: Gall-bladder Disease in Young Subjects, Surg., Gynec. & Obst. **46:** 795, 1928.
34. Else, J. E.: Quoted by Potter, A. H., 1928.
35. Eshner: Quoted by Potter, A. H., 1928.
36. Turcot, J.: Cholécystite et cholélithiase chez les jeunes; aspect étiologique, Laval méd. **10:** 338-343, 1945.
37. Vollmer, H.: Cholecystitis im Kindesalter, Ztschr. f. Kinderh. **49:** 200-201, 1930.
38. Berk, J. Edward: Acute Cholecystitis, in Bockus, H.: Gastroenterology, Vol. 3, Philadelphia, 1946, W. B. Saunders Company, page 534.
39. Cole, W. H., and Elman, R.: Textbook of General Surgery. Ed. 5, New York, 1948, D. Appleton-Century Company, pages 101, 648.

40. Judd, E. Starr, and Gray, H. K.: Cholecystitis and Cholelithiasis in Christopher, F., Textbook of Surgery. Ed. 5, Philadelphia, 1949, W. B. Saunders Company, page 1127.
41. Walters, W., Snell, A. M., and Clagett, O. T.: Surgery of the Biliary System. Lewis' Practice of Surgery, Vol. 7, Hagerstown, Md., 1948, W. F. Prior Company, Inc.
42. Deaver, Harry, C.: Cholecystitis Following Typhoid Fever in Children, Ann. Surg. **69:** 534-536, 1919.
43. Reid, M. R., and Montgomery, J. G.: Acute Cholecystitis in Children as a Complication of Typhoid Fever, Bull. Johns Hopkins Hosp. **31:** 7-11, 1920.
44. Mentzer, S. H.: A Clinical and Pathological Study of Cholecystitis and Cholelithiasis, Surg., Gynec. & Obst. **42:** 782, 1926.
45. Moxon: in Ewing, J.: Neoplastic Diseases, ed. 4, Philadephia, 1940, W. B. Saunders Company, page 753.
46. Erdmann, J. F.: Quoted by Mentzer, S. H., 1926.
47. Barrington-Ward, Sir Lancelot: The Abdominal Surgery of Children, ed. 2, London, 1937, Humphrey Milford, Oxford University Press.
48. Baty, James M., and Wagner, Richard: Diseases of the Gallbladder in Grulee, Clifford M., and Eley, R. C., The Child in Health and Disease, Baltimore, 1948, Williams & Wilkins Company, page 622.
49. Beals, J. A.: Cholecystitis and Cholelithiasis in Children, South. M. J. **21:** 666, 1928.
50. Bearse, C.: Gallstones in Patients Under 30 Years of Age, New England J. Med. **225:** 8-9, 1941.
51. Farr, C. E.: Cholecystitis and Cholelithiasis in Children, Arch. Pediat. **39:** 574-581, 1922.
52. Gairdner, D.: Association of Gall-Stones With Acholuric Jaundice in Children; Report of a Case in a Child Aged 3 Years With Note on Crisis of Acholuric Jaundice, Arch. Dis. Childhood **14:** 109-120, 1939.
53. Kellogg, E. L.: Gall-bladder Disease in Childhood, Ann. Surg. **77:** 587, 1923.
54. Matthews, F. S.: Gallstones in the Young, Ann. Surg. **59:** 781, 1914.
55. Montgomery, A. H.: Disease of the Gallbladder in Children, Am. J. Dis. Child. **44:** 372-378, 1932.
56. Shawan, H. K., and Long, E. C.: Gallbladder Disease in Young Children, Am. J. Surg. **21:** 43, 1933.
57. Sosnovik, I. I.: Characteristics of Gallbladder Disease at Various Ages and Biliary Lithiasis in Children, Vestnik khir. **58:** 123-130, 1939.
58. McClendon, S. J.: Gallstones in Children; a Case Diagnosed by Roentgen Examination, Am. J. Dis. Child. **45:** 584-586, 1933.
59. Melamed, L.: Die Duodenalsondierung bei den Erkrankungen der Gallenwege bei Kindern mit besonderer Berucksichtigung der Lambliase, Ann. paediat. **154:** 333-356, 1940.
60. Bird, Clarence E., Limper, Margaret A., and Mayer, Jacob M.: Surgery in Peptic Ulceration of Stomach and Duodenum in Infants and Children, Ann. Surg. **114:** 526, 1941.
61. Maingot, Rodney: Abdominal Operations, ed. 2, New York, 1948, Appleton-Century-Crofts, Inc.
62. Bachhuber, C. A.: Surgery of the Biliary Tract (Survey at L. A. General), M. Times, New York **68:** 3-7, 1940.
63. Heyd, C. G.: Analysis of 4,000 Operations for Gallbladder and Biliary Duct Disease, Rocky Mt. Med. Journal **45:** 119-129, 1948.
64. O'Shea, M. D.: Stones in the Ductus Choledochus; Analysis of 2,602 Cases of Biliary Tract Disease, Clinic at St. Vincent's and Harlem Hospitals, Am. J. Surg. **57:** 279-293, 1942.
65. Smith, B. C.: Acute Cholecystitis; Surgical Treatment of 332 Cases, S. Clin. North America **25:** 285-300, 1945.
66. Haggard, W. D., and Kirtley, J. A., Jr.: Manifestations of Gallbladder Disease, Analysis of 841 Operated Cases, J. Tennessee M. A. **32:** 126-132, 1939.
67. Fallis, L. S., and McClure, R. D.: Acute Cholecystitis; a Review of 320 Cases, Surg., Gynec. & Obst. **70:** 1022-1028, 1940.
68. Edington, G. H.: After-History of a Case of Gall-Stones in a Young Subject, Brit. M. J. **1:** 782, 1930.

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